Chairman Tom Davis. Thank you very much.

Members will have 7 days to submit opening statements for the record. We will now recognize our first panel: Dr. James LeDuc, the Director, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases at the Center for Disease Control and Prevention; Dr. Anthony Fauci, Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health; and Dr. Bruce Gellin, the Director of the National Vaccine Planning Office, Department of Health and Human Services.

As you know, it is the policy of this committee, we swear all witnesses in, so if you would rise and raise your right hands.

[Witnesses sworn.]

Chairman Tom Davis. Thank you. Be seated.

Dr. LeDuc, we will start with you and we will move straight down. Thank you very much.

STATEMENTS OF DR. JAMES W. LEDUC, DIRECTOR, DIVISION OF VIRAL AND RICKETTSIAL DISEASES, NATIONAL CENTER FOR INFECTIOUS DISEASES, CENTERS FOR DISEASE CONTROL AND PREVENTION; DR. ANTHONY FAUCI, DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH; DR. BRUCE GELLIN, THE DIRECTOR OF THE NATIONAL VACCINE PLANNING OFFICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES

STATEMENT OF DR. JAMES W. LEDUC

Dr. LeDuc. Thank you very much, Mr. Chairman and members of the committee.

I would like to share with you some of the advances that we have made on global surveillance. I will leave comments to the issues surrounding anti-viral drug development and vaccine development to my colleagues Dr. Fauci and Dr. Gellin.

Let me begin with a brief summary of the current situation in Asia. As of yesterday, June 28th, the World Health Organization had reported 108 cases of avian influenza in humans since January 28, 2004, with a case fatality rate of about 50 percent. The World Organization for Animal Health, the OIE, had confirmed H5N1 influenza infections in animals in nine Asian countries during 2004 and 2005, with especially severe outbreaks in Vietnam and Thailand. Although the situation is very serious, there remains no evidence for sustained human-to-human transmission.

We continue to work very closely with the World Health Organization to monitor the situation and indeed the Chief of our influenza branch, Dr. Nancy Cox, is en route back from Vietnam even as we speak, having just completed a mission to Hanoi as part of a WHO team to investigate a cluster of human cases of influenza.

CDC is working closely with health officials in the region to strengthen influenza surveillance capacity. In the last fiscal year, the department provided $5.5 million to WHO and countries of the region to establish or improve their national influenza centers and to strengthen the WHO global network of collaborating laboratories. The goal of these investments is to ensure the earliest possible recognition of strains with pandemic potential to make certain...
that the viruses are isolated and made available to the global community for vaccine development, and to assist countries in local control of efforts to prevent widespread transmission.

As part of these efforts, CDC staff are being assigned to the WHO office in Geneva and the regional office in Manila and in the country office in Vietnam. These investments are being leveraged through collaborations with the U.S. Navy laboratories in Indonesia and in Cairo, Egypt and with the CDC International Emerging Infections Program in Bangkok, Thailand. The fiscal year 2005 funding for this effort is $7.2 million. Recently, Congress passed and the President signed a fiscal year 2005 emergency supplemental appropriation which included $25 million in assistance to prevent and control the spread of avian influenza in Southeast Asia. These funds will further support development of improved disease surveillance, training of laboratory and medical staff, preparedness activities, and enhanced communication capabilities.

Here in the United States, we are training laboratory staff in all 50 States to ensure their ability to diagnose avian influenza should it arise. We are expanding our network of sentinel physicians to more accurately monitor the spread of influenza during the flu seasons. CDC has also taken the lead in revising the department’s pandemic preparedness plan. The revision, which is scheduled for release later this summer, will be significantly expanded and will provide comprehensive guidance to our partners in State and local health departments. The plan is being developed in cooperation with the Advisory Committee on Immunization Practices and the National Vaccine Advisory Committee, and will offer guidance on prioritization for use of both anti-viral drugs and vaccines.

Finally, CDC is leveraging investments already made in bioterrorism preparedness to ensure that these resources that are already part of the strategic national stockpile are included in our pandemic planning. Mass casualty and surge capacity planning for hospitals is also underway in conjunction with HRSA.

Health and Human Services Secretary Mike Leavitt has made influenza pandemic planning and preparedness a top priority and has chartered the Influenza Preparedness Task Force to prepare the United States for this potential threat to the health of our Nation. As a member of this task force, CDC is proud to undertake these activities with our partners both domestically and globally.

Thank you for the opportunity to share this information with you. I would be happy to answer any questions.

[The prepared statement of Dr. LeDuc follows:]
Testimony
Before the Committee on Government Reform
United States House of Representatives

The Next Flu Pandemic: Evaluating U.S. Preparedness

Statement of
James W. LeDuc, Ph.D.
Director,
Division of Viral and Rickettsial Diseases
National Center for Infectious Diseases
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U.S. Department of Health and Human Services

For Release on Delivery
Expected at 10:00 a.m.
Thursday, June 30, 2005
Mr. Chairman and members of the Subcommittee, I am pleased to be here today to describe planning and preparedness for an influenza pandemic, including the potential threat posed by the H5N1 avian influenza virus currently circulating in Asia. Department of Health and Human Services (DHHS) Secretary Mike Leavitt has made influenza pandemic planning and preparedness a top priority. Agencies within DHHS are working together formally through the Influenza Preparedness Task Force that Secretary Leavitt has chartered to prepare the United States for this potential threat to the health of our nation.

I will discuss steps the Centers for Disease Control and Prevention (CDC) is taking as a member of this Task Force and with many other partners both domestically and globally. The strength and flexibility of CDC and other components of the public health system are vital assets as the U.S. sharpens its readiness for an influenza pandemic. Although we have made significant progress, more work is needed, particularly in the areas of surveillance capacity and response, and in the development of potential vaccines. Increased public awareness and understanding about infection control, community containment and travel, and other actions also are important in preparation for an influenza pandemic.

In discussing pandemic influenza, I want to emphasize that the issues of pandemic influenza and inter-pandemic influenza (so-called “annual influenza”) are inextricably linked. The same laboratories, the same health care providers,
the same surveillance systems, and the same health department plans and personnel will guide both responses. Making sure that these people and organizations can address inter-pandemic influenza is our best overall hope for making sure the U.S. is prepared for an influenza pandemic.

Pandemics in Perspective

Inter-pandemic influenza causes an average of 36,000 deaths each year in the U.S., mostly among the elderly and nearly 200,000 hospitalizations. In contrast, the severity and impact of the next pandemic, whether from H5N1 or another influenza virus, cannot be predicted. However, modeling studies suggest that, in the absence of any control measures, a “medium-level” pandemic in the U.S. could result in 89,000 to 207,000 deaths, between 314,000 and 734,000 hospitalizations, 18 to 42 million outpatient visits, and another 20 to 47 million people being sick if 15 percent to 35 percent of the U.S. population develops influenza in a pandemic. The associated economic impact in our country alone could range between $71.3 and $166.5 billion. A more severe pandemic, as happened in 1918, could lead to much greater damage.

There are several important points about influenza and pandemic influenza.

- A pandemic could occur anytime during the year and could last much longer than inter-pandemic influenza, with waves of infection during the pandemic period.
• At some point in a pandemic, the capacity to intervene and prevent or control transmission of the virus can become extremely difficult because the size of the population that is infected becomes too large.

• Right now, the H5N1 avian influenza strain circulating in Asia among birds is considered the leading candidate to cause the next pandemic. However, it is possible for another influenza virus, and not H5N1, to cause the next pandemic. While we believe some viruses are more likely than others to cause a pandemic, we cannot predict with certainty the risks from specific viruses.

• We often look to history to try and understand how a modern pandemic might affect us and how we might intervene most effectively. However, there have been many changes since the last pandemic in 1968, including changes in population and social structures, medical and technological advances, and the increase in international travel. Some of these changes have increased our ability to handle pandemics, but other changes have made us more vulnerable.

• Because pandemic influenza viruses will emerge in part or wholly from among animal influenza viruses, such as birds, it is critical for human and animal health authorities to coordinate activities such as surveillance and to share relevant information as quickly as possible.

The Current Avian H5N1 Influenza Situation in Asia
For an influenza virus to cause a pandemic, it must (1) be a virus to which there is little or no pre-existing immunity in the human population; (2) be able to cause illness in humans; and (3) have the ability for sustained transmission from person to person. So far, the H5N1 virus circulating in Asia meets the first two criteria but has not yet shown the capability for sustained transmission from person to person.

Although the present avian influenza H5N1 strain in Asia does not yet have the capability of sustained person-to-person transmission, at least 100 persons have been infected, largely by having some form of contact with infected poultry, primarily chickens. In addition, a limited number of persons have been infected by very close contact with another infected person, but this type of transmission has not led to sustained transmission or large outbreaks. As of June 17, 2005 the World Health Organization (WHO) had confirmed 107 cases of H5N1 influenza in humans since January 28, 2004, with a case fatality rate of 51 percent. The World Organization for Animal Health (OIE) confirmed, as of June 8, 2005, that H5N1 had been found in animals from nine Asian countries in 2004 and 2005, with especially large outbreaks among animals in Vietnam and Thailand. Millions of domestic birds have been culled in attempts to stop the spread of the virus among animal populations. In addition to poultry, infections among migratory birds may have also been found since 2002.
At this point, the H5N1 strain now appears to be endemic in poultry and other birds in a number of Asian countries. This situation poses a threat to humans because H5N1 from such sources can continue to infect people and because persistence of H5N1 in these populations provides the virus with chances to mutate or reassort its genes with genes from other viral strains and create H5N1 viruses that can transmit easily among people. Recent studies also have found that domesticated ducks can appear healthy but carry and shed the H5N1 strain, allowing the virus to spread invisibly to other species. H5N1 also has been shown to naturally infect mammals, which is a particular concern because this increases the potential for H5N1 viruses to reassort with other influenza strains that already have the ability to spread among humans and other mammals. Studies have documented H5N1 infections of pigs, tigers, and leopards in Asia.

To monitor H5N1 viruses for changes indicating an elevated threat for people, we must continue to strengthen and build effective in-country surveillance, which includes enhancing the training of laboratorians, epidemiologists, veterinarians, and other professionals, and promoting the comprehensive reporting that is essential to monitor H5N1 and other strains of highly pathogenic avian influenza.

**Responding to a Pandemic**

Although the current situation is very serious, it remains relatively localized to Asia. However this situation could evolve into a pandemic, in which case the entire world's population would be at risk for developing pandemic disease. An
effective response to an influenza pandemic requires highly collaborative planning, implementation, and flexibility in resolving issues at many levels. DHHS is leading the coordination of preparedness efforts through its Pandemic Influenza Response and Preparedness Plan, which was released in draft form in August 2004 for public comment and is under revision. In addition, states are either developing pandemic influenza plans or revising existing plans to reflect new information and data. Key elements of these plans include the use of surveillance, infection control, antiviral medications, community containment measures, vaccination procedures, communications, and an ability to sustain essential services in times of widespread illness. To support the federal and state planning efforts, CDC is developing detailed guidance and materials for states and localities, and this guidance will be incorporated into the revised DHHS plan. CDC also is taking a lead role in working with the Advisory Committee on Immunization Practices and the National Vaccine Advisory Committee to recommend prioritized target groups for use of antiviral medications and vaccines during a pandemic when supplies are limited.

In the earliest pandemic stages, isolation precautions for persons who are ill and quarantine for persons exposed probably will be needed to try and limit the spread of pandemic influenza and to obtain as much time as possible for producing supplies of a pandemic vaccine. These control measures will require interventions such as the evaluation of ill travelers. Certain steps have been taken or will be taken to facilitate such efforts. On April 1, 2005, the President
amended Executive Order 13295, adding influenza caused by novel or reemergent influenza viruses that are causing, or have the potential to cause, a pandemic to the list of quarantinable diseases. CDC will implement travel notices to minimize the potential for infection to rapidly spread. Recently, CDC expanded the number and capacity of its quarantine stations at major ports of entry into the U.S. As with any quarantine, such activities need to be undertaken judiciously to minimize adverse effects on civil liberties.

Vaccination is the best overall, long-term strategy to reduce disease from inter-pandemic influenza outbreaks and pandemics. Antiviral medications, which can be used to prevent influenza and in some instances to treat influenza, provide another line of defense. These types of measures, together with those such as isolation of ill persons and quarantine of healthy exposed persons, help form a comprehensive preparedness approach both to address inter-pandemic influenza and to lay the foundation for responding to pandemic influenza.

Surveillance

Surveillance is critical for detecting and monitoring all infectious disease threats. Because early detection means having more time to respond, it is critical for the U.S. to work with domestic and global partners to expand and strengthen the scope of early-warning surveillance activities used to detect the next pandemic. We do not know how long it will take for pandemic disease in another country to spread to the U.S., but it could be a matter of days to months. And yet, months
of time, at best, will be needed to develop, produce, test, and administer vaccine to the entire U.S. population. Vaccine will be in short supply at the start of the pandemic and under the most favorable conditions, many will have become ill or died by the time the first dose of vaccine would be available to be given to the first person in this country. Global surveillance will also be used to monitor ongoing changes in a pandemic virus and thus allow us to know when the vaccine should be updated.

The outbreaks of avian influenza in Asia have highlighted several gaps in global disease surveillance that the U.S. must help address to improve our ability to prepare for an influenza pandemic. These limitations include (1) a lack of infrastructure in many countries for in-country surveillance networks; (2) the need for better training of laboratory, epidemiologic, and veterinary staff; and, (3) the resolution of longstanding obstacles to rapid and open sharing of surveillance information, specimens, and viruses among agriculture and human health authorities in affected countries and the international community.

In the past year, CDC and DHHS have made significant progress toward enhancing surveillance in Southeast Asia. However, this initiative needs to continue at both national and international levels if we are to sustain our progress, expand geographic coverage, and develop an adequate capacity to conduct effective surveillance. These efforts at building international as well as domestic surveillance are essential for detecting new influenza virus variants.
earlier and making informed vaccine decisions for inter-pandemic influenza. With the ever-present threat of the emergence of a new pandemic strain, we need to know what is happening in commercial poultry farms and the family backyard flocks of Southeast Asia, as well as elsewhere throughout the world.

Recently, Congress passed and the President signed an FY 2005 Emergency Supplemental Appropriations Act for Defense, the Global War on Terror, and Tsunami Relief, which included $25 million in international assistance funds to prevent and control the spread of avian influenza in Asia. These funds will support disease surveillance among humans, laboratories, and training on avian influenza laboratory and field techniques in Asia. They are being provided both to the region of Southeast Asia and to six specific nations where human and/or animal disease is greatest. Funding will support the planning and preparedness needed to enable each country to carry out a rapid response in a more organized manner. National long-term planning is also necessary for these countries; therefore they must also strategically apply to non-governmental organizations for additional funds to complete their preparedness efforts. Funds are also being provided for three countries, Cambodia, Laos, and Vietnam, to conduct active case detection of human disease, and additionally to Burma, China, and Indonesia for detection of animal disease. With respect to Burma, any avian flu assistance activities would be channeled through international non-governmental organizations or be conducted by international health organizations and not through the Burmese government. We will be happy to brief Congress on the
specific activities that will involve Burma. Improved laboratories, including addressing biosafety for animal and human specimens will be the initial focus. Better in-country communications will be developed to assist these populations to taking steps to prevent infection and disease. Direct assistance to Vietnam will provide technical help for the safe development of an H5N1 vaccine. Finally, rapid response teams for Vietnam, Cambodia, and Laos will be organized and trained to respond to a crisis by identifying disease and instituting quarantine, isolation, and any other control measures that are necessary. These teams will be supplied with materials to be stockpiled in Southeast Asia, so that they will be equipped with proper personal protective equipment when they conduct case investigations.

On the domestic side, during the past year, CDC has considerably improved surveillance in this country by working with the Council for State and Territorial Epidemiologists (CSTE) to make pediatric deaths associated with laboratory confirmed influenza nationally notifiable, and by implementing hospital-based surveillance for influenza in children at selected sites. CDC will continue to work with CSTE to make all laboratory confirmed influenza hospitalizations notifiable. Since 2003, we have issued interim guidelines to states and hospitals for enhanced surveillance to identify potential H5N1 infections among travelers from affected countries, and these enhancements continue. CDC also has been holding special laboratory training courses to teach state laboratory staff how to
use molecular techniques to detect avian influenza. CDC has trained professionals from all 48 states that desired training.

In addition, we are working to: (1) ensure that states have sufficient epidemiologic and laboratory capacity both to identify novel viruses throughout the year and to sustain surveillance during a pandemic; (2) improve reporting systems so that information needed to make public health decisions is available quickly; (3) enhance systems for identifying and reporting severe cases of influenza; (4) develop population-based surveillance among adults hospitalized with influenza; and, (5) enhance monitoring of resistance to current antiviral drugs, to guide policy for use of scarce antiviral drugs.

Managing the Vaccine Supply

During an influenza pandemic, the presence of influenza vaccine manufacturing facilities in the U.S. will be critically important. The pandemic influenza vaccines produced in other countries are unlikely to be available to the U.S. market, because those governments have the power to prohibit export of the vaccines produced in their countries until their domestic needs are met. The U.S. vaccine supply would be particularly fragile; only one of three influenza vaccine manufacturers selling vaccine in the U.S. market makes its vaccine entirely in the U.S.
In the U.S., public demand for influenza vaccine varies on a yearly basis, but having a steadily increasing demand would provide companies with a reliable, growing market that would be an incentive to increase production. In FY 2006, DHHS and CDC have provided $40 million in new funds for purchasing influenza vaccine for the pediatric stockpile to protect against annual outbreaks of influenza, and $30 million for contracts to expand the production of bulk single-strain influenza vaccine for use if needed during annual influenza seasons or possibly in a pandemic situation. In addition, the President is requesting $120 million in FY 2006, an increase of $21 million, to encourage greater production capacity that will enhance the U.S.-based vaccine manufacturing surge capacity to help prepare for a pandemic and further guard against annual shortages.

DHHS also appreciates the inclusion of $58 million in the FY 2005 Emergency Supplemental to procure additional influenza countermeasures for the CDC Strategic National Stockpile (SNS) in FY 2005. At present, the H5N1 viruses isolated from people in Asia during the past two years appear resistant to one class of antiviral drugs but sensitive to oseltamivir (Tamiflu). Accordingly, the SNS has stockpiled enough oseltamivir (Tamiflu) capsules to treat approximately 2.26 million adults and oseltamivir (Tamiflu) suspension to treat nearly 110,000 children. With the increased funding, CDC plans to purchase an additional 2 million regimens of oseltamivir. In addition, SNS funds have been used to purchase approximately 2 million bulk doses of unfinished, unfilled H5N1
vaccine. This vaccine has not yet been formulated into vials, nor is the vaccine licensed. Clinical testing to determine dosage and schedule for this vaccine began in April 2005 with funding from the National Institutes of Health. Additionally, DHHS also is supporting the development and testing of potential dose-sparing strategies that potentially could allow a given quantity of vaccine stock for use in more people.

One of the main efforts by CDC is to expand the nation’s use of influenza vaccine during inter-pandemic influenza seasons. This increase will help assure that the U.S. is better prepared for a pandemic. Influenza vaccine demand drives influenza vaccine supply. Therefore, if we can increase annual vaccination efforts, we will increase annual production efforts, which help strengthen our capacity for vaccine production during a pandemic. Discussions are under way to review the studies that would be needed to consider broadening recommendations for influenza vaccination. CDC also is developing strategies to increase influenza vaccine demand and access by persons who are currently recommended to receive vaccine each year. For example, according to a 2003 Institute of Medicine report, there are approximately 8.2 million uninsured adults 18-64 years with high-risk conditions warranting vaccination against influenza. If such persons receive influenza vaccine, it will help to increase annual demand for vaccine, because one of the best predictors of being vaccinated is having been vaccinated in a previous season. This increase in annual demand will lead
to increased production capacity, and thereby increase vaccine supply both annually and during a pandemic.

Additionally, for planning purposes, CDC has identified influenza vaccine supply scenarios that may occur in future influenza seasons. These scenarios range from worst-case to best-case situations and are an important part of CDC planning efforts. We are preparing recommendations, plans, and communication messages for each of these possible situations.

Conclusion

Although the present avian influenza H5N1 strain in Southeast Asia does not yet have the capability of sustained person-to-person transmission, we are concerned that it could develop this capacity. CDC is closely monitoring the situation in collaboration with the World Health Organization and the affected countries. CDC is using its extensive network of partnerships with other federal agencies, provider groups, non-profit organizations, vaccine and antiviral manufacturers and distributors, and state and local health departments to enhance pandemic influenza planning. Our responses to the annual domestic influenza seasons provide the core foundation for how the nation will face and address pandemic influenza.

Thank you for the opportunity to share this information with you. I am happy to answer any questions.
Chairman Tom Davis. Thank you.
Dr. Fauci.

STATEMENT OF DR. ANTHONY S. FAUCI

Dr. Fauci. Thank you very much, Mr. Chairman and members of the committee, for allowing me to discuss with you this morning the role of the NIH research endeavor in the ultimate development of countermeasures against pandemic flu in the form of diagnostics, therapeutics and vaccines.

Very briefly to put this into perspective, this slide here on your left shows the complementary roles within the Department of Health and Human Services. You have just heard from Dr. LeDuc about the CDC’s role in surveillance, detection, disease control and prevention. The NIH, as I will outline briefly for you, conducts basic and clinical research ultimately to develop vaccines and therapeutics. There is an important role for the FDA in the regulatory process of the approval of these products. This is all coordinated under the Office of Public Health Emergency Preparedness.

Next slide. The research enterprise at NIH is based fundamentally as are all of our projects on sound basic research that we hope to rapidly apply to the clinical setting of developing in this case vaccines and therapeutics. We do a bit of surveillance and epidemiology at the molecular level to look at the evolution of the virus, but the surveillance is fundamentally the responsibility of the Centers for Disease Control and Prevention.

I am going to give you a couple of examples of some of the basic and clinical research that is done, if I could have the next slide. You may have heard of the terminology “reverse genetic system.” This is a system of being able to much more accurately and consistently develop seed viruses for vaccines.

It may appear to be somewhat complicated, but it really is very simple. When we have a virus that we isolate, for example, in Asia that we want to make a vaccine for, we generally co-grow it with a strain that we know works well in eggs and that we have a great deal of experience with. During that process, the genes re-assort and ultimately give us a good growing, but nonetheless specific virus.

Reverse genetics deliberately takes the appropriate genes from each of those strains and re-combines them in a proactive way to take away the uncertainty. In fact, the vaccine that I am going to mention in a moment, the H5N1, was isolated and developed into a seed virus using reverse genetics technique. Next slide.

In addition, we, together with the CDC and in collaboration with several of the pharmaceutical companies, are working to make the transition from the egg-based system of developing a vaccine for influenza to a cell-based culture. The reasons for that are several, but the most important of which is the greater surge capacity of the cell-based system to be able to make more doses on a shorter notice, as well as to change direction if in fact we have a surprise virus that comes upon us. Next slide.

Probably the most important component of what we do relates to the actual clinical trials and testing of the vaccine in question. I must say that in fact we have been the first and are still way ahead of the rest of the world in the development of an H5N1 vac-
cine that is taking place in our clinical trial sites in this country to determine safety and the correct dose. Next slide. Very briefly, the H5N1 inactivated virus trial was started on April 5, 2005. We have completed the first two stages on 450 people. The dosage data, it will be done in multiple doses and in a prime boost will be available for analysis by mid-July. The safety data will be available for analysis by mid to end of August.

In addition, we are doing an attenuated vaccine trial that is planned for late 2005 for the H5N1. We are also studying another bird flu that is not as ominous as the H5, but nonetheless important, and that is the H9N2.

With regard to therapy, we have an anti-viral screening program. There are two major classes of drugs. The amantadine group, unfortunately the H5N1, that is circulating in Asia now is resistant to that. We can talk about why that might be the case during the question period. The other is the group that is the neuraminidase inhibitors, including Tamiflu. We are also looking for other alternative targets, as well as looking at how to use these drugs in combination where there are resistant scenarios, in addition to how to best use these drugs in different categories of patients.

On the final slide, let me just summarize that the NIH’s effort is fundamental research, as I mentioned. It is all geared to the rapid and expeditious development of the important countermeasures that are needed to counter a pandemic flu.

I would be happy to answer questions during the question period. Thank you, Mr. Chairman.

[The prepared statement of Dr. Fauci follows:]
Testimony
Committee on Government Reform
United States House of Representatives

The Role of NIH Biomedical Research in Pandemic Influenza Preparedness

Statement of
Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
U.S. Department of Health and Human Services

For Release on Delivery
Expected at 10:00 AM
Thursday, June 30, 2005
Introduction

Mr. Chairman and Members of the Committee, thank you for the opportunity to discuss with you the role of the National Institutes of Health (NIH) in preparing the Nation for the next influenza pandemic. The Department of Health and Human Services (DHHS) Draft Pandemic Influenza Preparedness and Response Plan outlines a coordinated national strategy to prepare for and respond to an influenza pandemic, and assigns specific roles to various Federal agencies; the National Institute of Allergy and Infectious Diseases (NIAID) holds the primary responsibility for carrying out those duties assigned to NIH.

In this capacity, NIAID provides the scientific input required to facilitate the development of both new influenza vaccine technologies and novel antiviral drugs against influenza viruses. Under this Administration, we have made extraordinary progress. DHHS has been investing in new technologies, securing more vaccines and medicines, and preparing stronger response plans. Total NIH funding for influenza research has grown more than five-fold in recent years, from $20.6 million in FY 2001 to an estimated $119 million in FY 2005. This is part of the largest investment ever made by the Federal government in protecting against influenza.

Influenza epidemics typically occur during the winter months in the United States and other temperate regions of the world and cause significant morbidity and mortality. On average, 36,000 people in this country die each year and 200,000
are hospitalized due to influenza and influenza-related complications. Each year, influenza viruses undergo small changes in their surface proteins as they circulate through the human population. As these small changes accumulate, the influenza virus gains the ability to overcome immunity created by prior exposure to older circulating influenza viruses or by vaccination. This phenomenon, called "antigenic drift," is the basis for the well-recognized patterns of influenza disease that occur every year, and is the reason that influenza vaccines must be updated each year.

Influenza viruses also can change more dramatically; viruses may emerge that can jump species from natural reservoirs such as wild ducks to infect domestic poultry, farm animals, or humans. This type of significant change in the antigenic makeup of the virus that infects humans is referred to as "antigenic shift."

In most instances when an influenza virus jumps species from an animal such as a chicken to infect a human, the result is a "dead end" infection that cannot readily be transmitted further from human to human. Mutations in the virus, however, could increase the efficiency of human-to-human transmission. Furthermore, if an avian influenza virus and another human influenza virus were to simultaneously co-infect a person, the genes of the two viruses might reassort, resulting in a virus that is readily transmissible between humans and against which the population would have no natural immunity. Such a virus could potentially cause an influenza pandemic.
Historically, pandemic influenza is a proven threat. Three influenza pandemics have occurred in the 20th century: in 1918, 1957, and 1968. The 1918-1919 pandemic was by far the most severe, killing over 500,000 people in the United States and 20-40 million people worldwide—almost two percent of the global population at that time. Worldwide, the pandemics that began in 1957 and 1968 killed approximately 2 million and 700,000 people, respectively.

H9N2 and H5N1 influenza are two avian viruses that have jumped directly from birds to humans and have significant pandemic potential. In 1999 and 2003, H9N2 influenza caused illness in three people in Hong Kong and in five individuals elsewhere in China, but the virus did not spread from human to human. H5N1 influenza, often referred to as "bird flu," appears to be a significantly greater threat than H9N2. This virus was first detected in humans in Hong Kong in 1997. Since January 2004, it has spread widely among wild and domestic birds and has infected at least 107 people in Vietnam, Thailand, and Cambodia; 54 of these people have died of the disease. Ominously, H5N1 viruses are evolving in ways that increasingly favor the start of a pandemic, including becoming more stable in the environment and expanding their host species range. Moreover, there have been 2 highly probable cases of human-to-human transmission of the H5N1 virus, and it is possible that other such transmissions have occurred recently.

The deadly experience with past influenza pandemics explains our current high level of concern about the appearance of virulent H5N1 avian influenza viruses in
Asia, which by a variety of mechanisms could adapt themselves to efficiently spread from human to human and result in the next pandemic. Given the poor condition of public health systems in many underdeveloped regions and the speed of modern air travel, the consequences of such an event, should it result in an influenza pandemic, would be severe.

**NIH Influenza Research Activities**

Between influenza pandemics, when influenza activity occurs regularly on a seasonal basis, the role of NIAID is to conduct basic research into the viral biology, pathogenesis, and epidemiology of influenza viruses and to study host immune responses to these agents. Concomitant with these basic research studies, NIAID conducts applied research to develop new or improved influenza vaccines and production methods; to identify new anti-influenza drugs; and to support surveillance for previously unknown influenza viruses in animals and characterize any that are found. When a new influenza virus begins to infect humans (and thereby gains the potential to cause a pandemic), NIAID’s role is to develop and clinically evaluate specific candidate vaccines against the emergent strain, assess the virus’s sensitivity to antiviral drugs, and, in some cases, supply vaccine manufacturers and the research community with viral reference strains and other reagents to speed vaccine development.

**Basic Research**

NIAID supports many basic research projects intended to increase our understanding of how influenza viruses replicate, interact with their hosts,
stimulate immune responses, and evolve into new strains. Results from these studies lay the foundation for the design of new antiviral drugs, diagnostics, and vaccines, and are applicable to seasonal epidemic and pandemic strains alike.

NIAID also supports two special research programs to better understand the diversity of influenza viruses. The Influenza Genome Sequencing Project, launched in the fall of 2004, is a collaboration between NIAID, the Centers for Disease Control and Prevention (CDC) and several other organizations to determine the complete genetic sequences of thousands of influenza virus isolates and to rapidly provide these sequence data to the scientific community. This program will enable scientists to better understand the emergence of influenza epidemics and pandemics by observing how influenza viruses evolve as they spread through the population and by matching viral genetic characteristics with virulence, ease of transmissibility, and other clinical properties. As of June 8, 2005, 206 genomic sequences of influenza viruses had been made available through this program to researchers via the NIH website, and many more are in the pipeline.

NIAID also supports a long-standing program based in Hong Kong to detect the emergence of influenza viruses with pandemic potential. This program, led by Dr. Robert Webster of St. Jude Children’s Research Hospital in Memphis, Tennessee, conducts extensive surveillance of influenza viruses in animals in Hong Kong, analyzes new influenza viruses when they are found, and helps to
generate candidate vaccines against them. In January 2005, the scope of this surveillance program was expanded to include Vietnam, Thailand, and Indonesia.

**Vaccines**

Vaccines are essential tools for the control of influenza. NIAID supports numerous research projects and other initiatives to foster the development of new influenza vaccine candidates and manufacturing methods that are simpler, more reliable, yield more broadly cross-protective products, and provide alternatives to the egg-based technology currently used to grow the vaccine viruses.

In the Fiscal Year 2006 budget request, DHHS has requested $120 million to support pandemic influenza preparedness activities. These activities build on previous initiatives that include making chicken eggs available year round to provide for a secure supply and surge capacity for vaccine production and supporting efforts to shift vaccine manufacture to new cell-culture technologies. Moreover, a technique developed by NIAID-supported scientists called reverse genetics allows scientists to manipulate the genomes of influenza viruses and to transfer genes between viral strains. This technique allows the rapid generation of vaccine candidate strains that precisely match a selected epidemic strain. By removing or modifying certain virulence genes, reverse genetics also can be used to convert highly-pathogenic influenza viruses into vaccine candidates that
are safer for vaccine manufacturers to handle. Other strategies for influenza vaccines, including protein subunit and gene-based vaccines, also are being actively pursued. For example, on the NIH campus in Bethesda, the NIAID Vaccine Research Center (VRC) has initiated a program to develop gene-based vaccines against influenza. Should proof-of-concept studies prove successful, the VRC expects to expand and accelerate the development of gene-based and recombinant influenza vaccines.

In addition to supporting the development of new vaccine strategies, NIAID maintains an extensive capacity for evaluating candidate vaccines in clinical trials. For example, NIAID's Vaccine and Treatment Evaluation Units (VTEUs) comprise a network of university-based research medical centers across the United States that conduct clinical trials to test candidate vaccines for many infectious diseases. These units support both academic and industrial vaccine evaluation, including safety, immunogenicity, and ultimately, efficacy of candidate vaccines.

Although a pandemic alert has not yet been declared, NIAID has taken a number of steps to develop and clinically test vaccines against H5N1 and H9N2 influenza, two specific avian viruses that, as noted above, have significant pandemic potential. For example, in August 2004, NIAID contracted with Chiron Corporation for the production of 40,000 doses of an inactivated H9N2 vaccine.
A Phase I clinical trial of this vaccine in adults began on March 31, 2005, and is fully enrolled.

In January 2004, researchers at St. Jude Children’s Research Hospital obtained a clinical isolate of the highly virulent H5N1 virus that continues to be fatal to humans in Vietnam and used reverse genetics to create an H5N1 vaccine candidate from this strain. After NIAID received this vaccine candidate last June, it was sent immediately to Sanofi-Pasteur (formerly Aventis-Pasteur) and shortly thereafter to Chiron. These companies have NIAID contracts to manufacture pilot lots of eight and ten thousand vaccine doses, respectively. The inactivated H5N1 vaccines will be tested in Phase I and II clinical trials that will assess safety and the appropriate vaccine dosage to optimize immunogenicity, as well as provide information about how the immune system responds to this vaccine. The Sanofi-Pasteur trial, which began on April 4, 2005, is testing the vaccine in approximately 450 healthy adults between the ages of 18 and 64. This trial is already fully enrolled. If data from this study indicate the vaccine is safe and able to stimulate a potentially protective immune response, NIAID expects to test the vaccine in other populations, such as the elderly and children, in late summer 2005. Trials of the Chiron-produced vaccines are expected to begin later this year.

In addition to these relatively small pilot lots, DHHS contracted with Sanofi-Pasteur to produce two million doses of its H5N1 vaccine, in order to ensure that
the manufacturing techniques, procedures, and conditions that would be used for large-scale production will yield a satisfactory product. Moving to large-scale production of the vaccine in parallel with clinical testing of pilot lots is an indication of the urgency with which we have determined that H5N1 vaccine development must be addressed. Waiting for the results of the initial clinical trials, which would be the normal procedure, would delay our ability to make large quantities of vaccine by at least six months. These doses, which have now been manufactured, could be used to vaccinate health care workers, researchers, and, if indicated, the public in affected areas.

From the mid 1970s to the early 1990s, intramural and extramural NIAID researchers developed a cold-adapted, live attenuated influenza vaccine strain that later became the FDA-licensed influenza vaccine marketed as FluMist. Building on their experience with attenuated influenza vaccines, researchers from the same intramural laboratory involved in previous efforts recently made three candidate attenuated H5N1 vaccine strains and an attenuated H9N2 vaccine strain that are now in advanced development. NIAID plans to start the clinical trial of the attenuated H9N2 candidate vaccine this summer. These researchers also hope to test one of the candidate attenuated H5N1 vaccines in a Phase I study this year.

Antiviral Therapies
Antiviral medications are an important counterpart to vaccines as a means of controlling influenza outbreaks, both to prevent illness after exposure and to treat infection after it occurs. Four drugs are currently available for the treatment of influenza, three of which are also licensed for prevention of illness. NIAID actively supports identification of new anti-influenza drugs through the screening of new drug candidates in cell culture systems and in animal models. In the past year, seven promising candidates have been identified. Efforts to design drugs that precisely target viral proteins and inhibit their functions also are under way. In addition, NIAID is developing novel, broad-spectrum therapeutics that might work against many influenza virus strains. Some of these target viral entry into human cells, while others specifically attack and degrade the viral genome.

Efforts also are underway to test and improve antiviral drugs to prevent or treat H5N1 influenza. Last year, researchers determined that although H5N1 viruses are resistant to two older drugs—rimantadine and amantadine—they are sensitive to a newer class of drugs called neuraminidase inhibitors, including oseltamivir, which is marketed as Tamiflu and is approved for use in individuals older than one year. DHHS has deposited approximately 2.3 million treatment courses of oseltamivir in the Strategic National Stockpile, to which more doses will be added. Scientists are planning to conduct studies to further characterize the safety profile of oseltamivir for very young children; and studies are also in progress to evaluate novel drug targets, as well as long-acting next-generation neuraminidase inhibitors. In addition, development and testing in animals of a
combination antiviral regimen against H5N1 and other potential pandemic influenza strains are under way.

Conclusion

In closing, Mr. Chairman, I would like to emphasize that although we cannot be certain exactly when the next influenza pandemic will occur, we can be virtually certain that one will occur and that the resulting morbidity, mortality, and economic disruption will present extraordinary challenges to public health authorities around the world. We are working diligently in close coordination with our colleagues at CDC, FDA, other federal agencies, and in industry to ensure that we can meet these challenges in the most successful manner possible.

Thank you for this opportunity to appear before you today, and I would be pleased to answer any questions that you may have.
The Role of NIH Biomedical Research in Pandemic Influenza Preparedness

U.S. House of Representatives Committee on Government Reform

Dr. Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Department of Health and Human Services
June 30, 2005
Pandemic Influenza Preparedness: Complementary Roles within DHHS

**CDC**
- Surveillance and detection
- Train local response teams
- Maintain vaccine/antiviral stockpiles
- Disease control/prevention

**NIH**
- Conduct basic research
- Develop medical interventions (vaccines, antivirals)
- Conduct clinical evaluation of vaccines and antivirals

**FDA**
- Regulatory approval – vaccines, therapeutics, diagnostics

**OPHEP**
- Office of Public Health Emergency Preparedness
  coordinates HHS-wide emergency preparedness activities
Influenza Seed Virus for Inactivated Virus Vaccine Production Using a Reverse Genetics System

Highly pathogenic H5 or H7

A/Puerto Rico/8/34 (H1N1)

Removal of additional basic amino acids

Vaccine approved cell line

Influenza Vaccine Production: Cell Culture as an Alternative to Chicken Eggs

Provide target viruses to vaccine manufacturers

Egg-based

Cell culture-based

Identify target influenza strains
Reuters
March 24, 2005

U.S. Starts Human Tests of Bird Flu Vaccine

Phase 1 trial on 450 adults will determine safety of shots

U.S. health officials said on Wednesday they have started human tests of a vaccine against avian flu, which experts believe could kill tens of millions of people if it becomes easily passed from person to person.
Clinical Trials for Pandemic Influenza

H5N1

- Inactivated vaccine trial began April 4, 2005
  - Stage 1: fully enrolled (118 healthy adults)
  - Stage 2: fully enrolled (333 healthy adults)
  - Upon review of safety and preliminary immunogenicity data, plan to conduct trials in healthy elderly and children in late summer 2005

- Attenuated vaccine trial planned for late 2005

H9N2

- Inactivated vaccine trial began March 31, 2005
  - Fully enrolled (96 healthy adults)

- Attenuated vaccine trial planned for summer 2005
Antiviral Therapies for Influenza

- Hemagglutinin (H)
- Neuraminidase (N)
- Oseltamivir
- Zanamivir
- M2 Protein
- Amantadine
- Rimantadine
NIH Influenza Research

Vaccines

Therapeutics

Diagnostics

Surveillance and Epidemiology

Basic Research

Expansion of Research Capacity
Chairman Tom Davis. Thank you very much.
Dr. Gellin.

STATEMENT OF DR. BRUCE GELLIN

Dr. Gellin. Thank you, Mr. Chairman and members of the committee. I am pleased to have the chance to discuss with you this morning the department’s involvement with avian influenza and the steps we are taking to prepare for a pandemic.

As you have mentioned in your remarks and you have heard from my colleagues this morning, many public health experts believe the threat of a pandemic is now greater than it has been in decades. A report by the World Health Organization warns that the H5N1 virus may be evolving in ways that increasingly favor the start of a pandemic.

The thin silver lining on this otherwise darkening cloud is that despite the wide geographic spread of the virus, despite its ability to infect an expanding number of avian and mammalian species, despite the small changes in the virus’ genetics, and despite the occurrence of small clusters among people where transmission may have been person to person, this virus has not yet developed the ability to efficiently transmit among people, a change that could trigger a pandemic.

While we are all focused on the evolving H5N1 situation, as Dr. Fauci mentioned, it is the nature of this virus to evolve. Therefore, we need to be prepared for any of these viruses that could do a similar thing.

Because the emergence of a pandemic anywhere could lead to a pandemic everywhere, this indeed is a global issue. It is why the department has made preparedness for an influenza pandemic one of its highest priorities. It is why it is a critical component of Secretary Leavitt’s 500-day plan. It is why Secretary Leavitt on his first international trip in May gave a plenary talk at the World Health Assembly, the annual meeting of the ministers of health around the world, and hosted a meeting of more than a dozen ministers of health in the affected region, reinforcing the need for global transparency, strengthened surveillance and communications, and timely sharing of information and clinical specimens.

It is also why Secretary Leavitt established a department-wide Influenza Task Force to coordinate all HHS activities affecting the public health preparedness for both seasonal influenza and pandemic. It is why HHS has made significant investments in adding influenza-specific medicines and vaccines to our strategic national stockpile, and why we are currently in active discussions with the manufacturers of these drugs and vaccines to obtain more.

It is also why we have supported the World Health Organization’s global influenza effort through both human and financial resources, and why we provide technical assistance and other resources through a number of bilateral agreements with countries in the affected regions.

And it is why we have collaborative working relationships with many other parts of the U.S. Government, including the Department of Agriculture, the Department of State, the USAID, the Department of Defense and the Veterans Administration, to name a few.
And it is why Secretary Leavitt has asked that the department complete the updated 2005 pandemic preparedness and response plan. This plan describes a coordinated strategy to prepare for and respond to a pandemic. The updated plan will address the outstanding policy issues and provide the guidance and specificity that is needed by local and State health departments, the health care community, the public and the international community. We anticipate that we will be regularly revising and reworking the plan that incorporates evolving science and experience.

With the broad area of pandemic influenza, the department’s priority areas include public health preparedness, surveillance, stockpiles of drugs and vaccines, vaccine development and advanced product development, and basic and applied research. Drs. LeDuc and Fauci have highlighted a number of these areas already, so in the few minutes that remain I would like to spotlight our approach to developing our armamentarium for pandemic antiviral drugs and vaccines.

As you know, last year we began to include anti-viral drugs in the strategic national stockpile. The bottom line is that today, neuraminidase inhibitor drugs are the only class of anti-virals that can take on this virus. It is worrisome that the other class, the M2 inhibitors or the adamantines are no longer effective. As recently reported in the Washington Post, it appears that the use of these anti-viral drugs in livestock feed are largely responsible for the emergence of resistance to this virus, underscoring the critical importance that these drugs be used appropriately so they will continue to work.

We are also exploring the potential to include other anti-viral drugs in our strategic national stockpile, including zanamivir, also known as Relenza. I would like to acknowledge our appreciation of Congress’ inclusion of the $58 million supplement so that we could procure these additional countermeasures for our stockpile.

In addition to anti-viral drugs for the treatment and prevention of influenza, vaccination is one of the most important tools that we have for pandemic preparedness. It is important to acknowledge that the perfect vaccine cannot be prepared in advance and stockpiled since the vaccine needs to be tailored to match the circulating virus.

We have gone ahead, as Dr. Fauci mentioned, and created a vaccine and we have 2 million potential doses that have been made in bulk waiting for the result of the NIH trial to know what dose should be used. This provides us with some vaccine that has potential use and also provides at least one vaccine manufacturer with significant experience working with this strain in commercial-scale facilities.

HHS has developed several other influenza vaccine supply initiatives that are designed to secure and expand the influenza vaccine supply, diversify our production methods such as cell culture, and establish emergency surge capacity. To support these activities, HHS received $50 million in fiscal year 2004, $99 million in fiscal year 2005, and in the current President’s budget, we have an additional $120 million to strengthen this component of our preparedness.
Our pandemic efforts include beyond the cell cultured vaccine that Dr. Fauci mentioned, efforts to improve the efficiency of the manufacturing process and approaches that could effectively stretch the number of vaccine doses by decreasing the amount of vaccine antigen in each dose. These dose-stretching strategies may be affected by the use of an adjuvant or administration such as interdermal administration.

While issuing the requests for proposals and completing the contracts is only the first step toward development of an expanded, diversified and strengthened vaccine supply, as Dr. Fauci mentioned, the United States is leading the global effort to develop vaccines and vaccine technologies to meet this challenge.

Thank you for our attention to my remarks, and I look forward to any questions you may have.

[The prepared statement of Dr. Gellin follows:]
Testimony
Before the Committee on Government Reform
United States House of Representatives

Pandemic Influenza Preparedness

Statement of
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U.S. Department of Health and Human Services

For Release on Delivery
Expected at 10:00 AM
Thursday, June 30, 2005
Mr. Chairman and members of the Committee, I am Dr. Bruce Gellin, Director of the National Vaccine Program Office at the Department of Health and Human Services and the Chair of the Secretary’s Influenza Preparedness Task Force. I am pleased to appear before you today to discuss avian influenza and the measures the Department is taking to prepare for an influenza pandemic.

An influenza pandemic is a global outbreak of disease that occurs when a new influenza A virus emerges in the human population, causes serious illness, and then spreads easily from person to person worldwide. Three influenza pandemics have occurred during the 20th century. The most deadly influenza pandemic outbreak was the 1918 Spanish flu pandemic, which caused illness in roughly 20 to 40 percent of the world’s population and resulted in at least 500,000 deaths in the United States and 20-40 million deaths worldwide.

Many public health experts believe the threat of a pandemic is now greater than it has been in decades. A report issued by the World Health Organization warns that the virus may be evolving in ways that increasingly favor the start of a pandemic. In addition, the ecology of the disease and behavior of the virus have changed and are creating multiple opportunities for a pandemic virus to emerge.

This is in large part because of the influenza H5N1 virus, the so-called “bird flu” that is established and endemic in many different species of birds in Asia. As these avian viruses continue to evolve and spread in animals, the possibility increases that an avian virus will recombine with a human virus to cause a novel and easily transmitted influenza virus strain in humans. Based on data that has
been made available to the World Health Organization on the impact of the H5N1 virus in Asia, more than half of the people who are known to have been infected with this virus have died from this infection. This is not an exact estimate of the mortality rate for this disease because only people who have become sick enough to go to the hospital have actually been diagnosed with the infection. There may be many more people who were infected without being diagnosed.

While scientists in 1918 had very little idea of what was happening until it was too late, we have time - and still have time - to prepare for the next global pandemic, and we should consider ourselves warned. As Secretary Leavitt stated at the World Health Assembly in May, "We are working on pandemic preparedness on borrowed time. When this event occurs, our response has got to be immediate, comprehensive and effective."

The Department has made preparedness for an influenza pandemic one of its highest priorities and it is a critical component of Secretary Leavitt’s 500-day plan. In May, at the World Health Assembly -- the annual meeting of Ministers of Health from around the world -- the Secretary spoke of the Department’s commitment in this area. He encouraged global transparency, strengthened surveillance and communications, and timely sharing of information and clinical specimens as a critical component of our global preparedness. Secretary Leavitt also urged international collaborations among developed and developing countries to control the virus among humans and animals. Further, the World
Health Assembly passed a resolution on pandemic preparedness that was originally offered by the U.S. as a blueprint for global action.

We have expanded and enhanced the planning and preparedness activities that are critical to improving the effectiveness of a national and worldwide response that would decrease the impact of a pandemic should it occur. HHS has increased support for pandemic influenza activities and is engaged in several efforts to enhance the nation's preparedness for such an outbreak. HHS supports pandemic influenza activities in several key areas including: public health preparedness, research, vaccine development and production, antiviral stockpiling, and surveillance.

In addition, on the national front, the Department has been actively revising the draft Pandemic Influenza Preparedness and Response Plan that was issued last year 2004. This Plan describes a coordinated strategy to prepare for and respond to an influenza pandemic. The 2005 update of the plan will address many of the outstanding policy issues and provide the guidance to state and local health departments, the healthcare system, the public and the international community. HHS will regularly be revising and reworking the plan in order to provide current thinking and current science.

Earlier this month, Secretary Leavitt established a Department-wide Influenza Task Force to coordinate all HHS activities affecting the public health
preparedness for seasonal influenza outbreaks and an influenza pandemic. The Task Force's near term objective is to ensure completion of an updated pandemic plan. Long term objectives include an effective and efficient global surveillance network for outbreaks of influenza-like illness in humans and animals, and interoperable local, state, and federal government response plans for influenza outbreaks within the United States -- including strategies and plans for effective coordination with response partners, public and private, and timely communication with the public.

To address the outstanding policy issues that will be incorporated into the Department's 2005 update of the Pandemic Preparedness and Response Plan, a joint working group of the National Vaccine Advisory Committee (NVAC) and Advisory Committee on Immunization Practices (ACIP) has been established to provide guidance to the Department. In addition to representatives from each of these federal advisory committees, working groups have had representation from public health and health care organizations, industry, federal agencies and other Departments. Next month, a joint meeting of NVAC and ACIP will review the findings of the working group and develop recommendations for prioritizing the use of pandemic vaccine and antiviral drugs.

In addition to the guidance embodied in the Department's Pandemic Influenza Preparedness and Response Plan, HHS is taking many proactive steps to prepare and plan for a pandemic. One of these critical elements is the inclusion
of antiviral drugs in the Strategic National Stockpile (SNS). Another component of our preparedness is ensuring sufficient domestic surge capacity for influenza vaccine production.

Influenza antiviral medications have long been used to limit the spread and impact of institutional influenza outbreaks. These drugs may serve an important role in stemming a developing pandemic and in treating patients early in their influenza infection, with greatest effect if the drug is administered within 48 hours of onset of symptoms. We plan to utilize antiviral drugs as one influenza countermeasure to help mitigate influenza impact. Laboratory analyses demonstrate that these drugs appear to have activity against the H5N1 influenza strains in Asia; however, we have limited data to date about their effectiveness in treating patients infected with this virus. To date, there are some anecdotal reports of human H5N1 infections that have advanced despite early treatment, but anecdotes are not data. We need better data from the field to guide our decisions.

It is worrisome that M2 inhibitors, one of only two classes of antiviral drugs for influenza is not likely to be useful in fighting the H5N1 virus. As reported recently in the Washington Post, it appears that the use of the antiviral drug amantadine (an M2 inhibitor) in livestock feed in Asia is responsible for the emergence of resistance to the virus. This underscores the critical importance, that these drugs
be used appropriately so as not to induce further resistance by the virus and removing this drug from our armamentarium.

The bottom line is that today, neuraminidase inhibitor drugs are the only class of antivirals available that can take on this virus. The United States has ordered and received delivery of approximately 2.3 million treatment courses of the antiviral, oseltamivir (Tamiflu®), a neuraminidase inhibitor, for the SNS and is currently in active discussions with Roche, the maker of this drug, to increase our national reserve. In addition, we are exploring the potential to include the other antiviral drug in this class, zanamivir (Relenza®), in the SNS. The Department also appreciates Congress' inclusion of $58 million in the FY 2005 Emergency Supplemental Appropriations Act for Defense, the Global War on Terror, and Tsunami Relief to procure additional influenza countermeasures for our Strategic National Stockpile.

In addition to antiviral drugs for the treatment or prevention of influenza, vaccination is one of the most important tools we have for pandemic preparedness, as it is the primary means to prevent morbidity and mortality during an epidemic. Because a pandemic is by definition the introduction and spread of a novel strain, there are major implications for vaccine development.

- First, the majority of the population is likely to be susceptible. NIH's clinical studies on the H5N1 vaccine will be available in the coming weeks and will provide critical information about the immune response and safety
profile of this candidate vaccine. Because humans’ immune systems have not encountered this novel virus before, we expect that two doses of a vaccine might be needed for effective immunity, but we will let the science speak for itself when the results of these clinical trials are available.

- In addition we need to ensure that we have adequate capacity to produce a vaccine once its proof of principle has been established. To this end, we recognize that modern transportation and trade are likely to rapidly accelerate the global spread of influenza. Given our experience with the infectiousness of influenza, we assume that an outbreak somewhere is very likely to become a health threat anywhere…and potentially everywhere. As a consequence, our planning assumption is that in the setting of a pandemic emergency, there will be worldwide demand for vaccine and therefore vaccine produced outside of the United States will not be available for domestic use.

From a preparedness perspective, it is important to acknowledge that that the perfect vaccine cannot be prepared far in advance and stockpiled, since the vaccine has to be tailored to match the circulating virus. In addition to the vaccine that has been developed for NIH’s clinical vaccine trials, we have asked Sanofi Pasteur develop 2 million doses of H5N1 vaccine based on the virus that was in circulation in Asia last year. We don’t yet know whether the H5N1 vaccine will provide protection against a pandemic strain that might emerge, but this action provides us with some vaccine that has potential use, while also providing
at least one manufacturer with significant experience working with this strain in commercial-scale manufacturing facilities and is likely to translate into time saved in the development of a pandemic vaccine should the need arise. It is possible that the pandemic virus will continue to evolve (drift), such that this vaccine could be a poor match for and have limited effectiveness against the circulating strain but we chose to take advantage of the narrow window of opportunity in the manufacturing cycle so that this vaccine could be made without interfering with the production of the annual influenza vaccine that is made in the same facility.

Developing and producing a pandemic vaccine is further compounded by a fragile vaccine supply system. This fragility was documented during the past influenza season, when one of the two large influenza vaccine manufacturers could not supply vaccine to the U.S. market. While we are optimistic that there are new influenza manufacturers coming to US market, these ongoing problems with annual influenza production highlight the need for greater diversification of the U.S. domestic production capacity and the parallel need to improve demand for a life-saving vaccine that remains underutilized.

All U.S. licensed influenza vaccines are developed from viruses that are grown in embryonated eggs in a process unique for influenza vaccine. Influenza vaccine manufacturing happens when a strain of the virus adapted to grow in eggs is injected separately into millions of fertilized eggs, which are subsequently incubated to allow the Influenza virus to grow. These egg-grown viruses are
inactivated, purified, tested for potency, blended into the trivalent vaccine, and filled into syringes or vials. The number of influenza vaccine doses produced is limited by the capacity of the production facilities, the availability of embryonated eggs, the yield of influenza virus from each egg, and the length of time that manufacturing takes.

HHS has developed several influenza vaccine supply initiatives to address annual as well as pandemic influenza vaccine. The objectives of these initiatives are to
- secure and expand U.S. influenza vaccine supply
- diversify production methods, and
- establish emergency surge capacity.

To support these activities, HHS received $50 million in FY2004 and $99 million in FY2005. The President's Budget for FY2006 includes an additional $120 million to further strengthen this component of the overall pandemic influenza preparedness efforts.

Because influenza vaccine is produced to meet the seasonal demand in the fall, production also is seasonal and embryonated eggs have not been available to manufacturers year-round. Moreover, although some excess supply may be available to support additional influenza vaccine production or provide security if the flocks that produce eggs for vaccine production are affected by avian influenza or other illness, this excess is limited creating vulnerability to supply
disruption. To enhance influenza vaccine supply security, HHS issued a five-year contract to Sanofi-Pasteur of Swiftwater, Pennsylvania, on September 30, 2004 for $40.1 million. Under this contract, Sanofi-Pasteur has begun to change its flock management strategy to provide a secure, year-round supply of eggs suitable for influenza vaccine production at full manufacturing capacity. It also will increase the number of egg-laying flocks by 20% to provide contingency flocks in case of an emergency. These eggs may be used to support additional production of annual influenza vaccine in the event of a vaccine shortage with the doses being delivered later in the fall. Additionally, this contract provides for production of annual investigational lots of prototype pandemic influenza vaccines. For example, this summer, Sanofi-Pasteur will manufacture an H7N7 virus vaccine that will be evaluated through the National Institutes of Health Vaccine Treatment and Evaluation Units.

Diversification of influenza vaccine production methods also will help strengthen the system. Cell culture technology is a well-established vaccine production method for other vaccines such as the inactivated poliovirus vaccine, and two companies have registered their cell-culture based influenza vaccine technology in Europe. This production technology does not require eggs as a substrate for growth of vaccine virus, thereby avoiding the vulnerabilities associated with an egg-based production system. It also may be more amenable to surge capacity production when influenza vaccine production will be needed to be expanded rapidly, such as at the time of a pandemic. Finally, the new cell-based influenza
vaccines will provide an option for people who are allergic to eggs and therefore unable to receive the currently licensed vaccines.

Earlier this spring, Secretary Leavitt announced that the Department of Health and Human Services issued a five-year contract on March 31, 2005 to Sanofi-Pasteur for $97.1 million to develop cell culture influenza vaccine technology and conduct clinical trials, with the goal of obtaining an FDA license for this vaccine. Under this advanced development contract, the company has also committed to manufacturing this vaccine at a U.S.-based facility with a capacity to manufacture 300 million doses of monovalent (single strain) pandemic vaccine over a one-year period. However, given timelines for vaccine development and clinical trials, and for construction and validation of manufacturing facilities, additional influenza vaccine supply from this source is unlikely to be available for at least five years.

These important steps to strengthen our national influenza vaccine supply through assuring the egg-supply and diversifying and expanding production capacity will be followed this year by additional measures to increase influenza vaccine production capacity and expand the number of influenza vaccine doses made using that capacity. Supported by the pandemic influenza vaccine initiative in the FY'06 budget request for $120 million, we posted synopses of three additional areas where we believe strategic investments move us toward achieving annual and pandemic influenza vaccine supply goals in the March 17, 2005 edition of FedBizOpps. On April 29, 2005, the first of those requests for
proposals was posted, providing support for the development of cell-culture
based and recombinant pandemic influenza vaccines. This contract, leading to
the licensure and U.S. production of a next-generation influenza vaccine, will
further increase production capacity and diversification of the manufacturing
base.

Whereas building new influenza vaccine production facilities is one approach to
expand the influenza vaccine supply, other strategies also can increase the
number of influenza vaccine doses produced. Influenza vaccine is manufactured
in a series of steps – developing an influenza virus master seed for vaccine
production, inoculating the virus into eggs, growing, harvesting, purifying,
splitting, formulating, and filling it into vials or syringes. Improving efficiency at
any step in this process can increase the eventual yield and number of vaccine
doses produced. Thus, a second area of emphasis will be to support
improvements of the manufacturing process to increase overall influenza vaccine
production at current manufacturing facilities.

The third area of emphasis will provide support for research and development,
leading to licensure of strategies that will stretch the number of vaccine doses
produced by decreasing the amount of influenza virus antigen that is needed in
each dose. The concept underlying these "dose-stretching" strategies is that by
changing either the influenza vaccine or the way it is administered, one can
improve the immune response to vaccination and provide protection while using
less of the vaccine antigen. By using less antigen in each vaccine dose, the number of doses that can be made at any level of production capacity would be multiplied. The two most promising antigen-sparing approaches are either to add an adjuvant (a substance that stimulates the immune response to a vaccine formulation), or administering the vaccine into the skin (similar to the approach used in a skin test for tuberculosis) where large numbers of potent immune cells are located. Both strategies have been evaluated in several clinical trials and have the potential to expand influenza vaccine supply several-fold if they prove effective in further clinical trials and are approved for licensure.

The increase in the FY 2006 President's Budget request will support ongoing activities to ensure that the Nation will have an adequate influenza vaccine supply to respond better to yearly epidemics and to influenza pandemics. While issuing the requests for proposals and completing the contracts is only the first step toward the development of an expanded, diversified, and strengthened influenza vaccine supply, the U.S. is leading the global effort to develop vaccines and vaccine technologies to meet this challenge.

Stemming the spread of the epidemic will require close coordination between the agriculture and health sectors and among affected countries, donor nations and international organizations dedicated to promoting the health of humans, livestock and wildlife. The FY 2005 Emergency Supplemental Appropriations Act for Defense, the Global War on Terror, and Tsunami Relief included $25 million
to prevent and control avian influenza in Southeast Asia. Detailed joint planning
is already underway with the Department of State (with HHS focusing on human
health) and USAID working (with USDA focusing on projects on animal health
and related issues). In this way, the two agencies' plans will be complementary,
not duplicative.

With this funding, we will support activities with the following goals:

- Strengthening the capacity of affected countries to conduct disease
  surveillance, prevention, and response, primarily in the most affected
  countries – Vietnam, Cambodia, and Laos
- Limiting the spread of the H5N1 avian influenza virus among birds.
- Limiting the spread of the H5N1 avian influenza virus from animals to
  humans.
- Reducing the potential economic consequences of avian influenza for
  affected countries.

The threat of a pandemic is real, whether it comes in 10 days or 10 years from
now and whether it is H5N1 or another emerging strain. In anticipation of the
next pandemic, we are working along with the global health community on this
public health threat. The US has taken a leadership role in this area. We
recognize the challenge before us, and know that we must all continue to be
diligent and prepare for a potential public health threat of unimaginable
magnitude.
Thank you for your attention to my remarks this morning – and more importantly to the attention that you have paid to pandemic influenza. I would be happy to answer any questions from the Committee.
Chairman Tom Davis. Thank you very much.

Dr. LeDuc, let me start. It is my understanding that we have two medical interventions for addressing a pandemic: a vaccine, which could take months to manufacture a sufficient quantity; or treatment with an anti-viral such as Tamiflu for those who get sick. At the moment, the United States has stockpiled only enough Tamiflu for 2 percent of the population. What, in your professional judgment, should be the level of the Tamiflu stockpile?

Dr. LeDuc. Clearly, Tamiflu has an important role to play in our national preparedness for the threat of pandemic influenza. It, however, is not our only resource. As you mentioned, vaccines are critically important. I think our strategy currently is to use anti-viral drugs through the early phase during which a vaccine would actually be made. I think our efforts to actively engage in the global community to recognize early on the threat of pandemic influenza and to shorten the timeline between getting access to that virus and creating the new vaccine is also a factor in our considerations.

I do not have a number to give you. I would probably get in big trouble if I put forward a number anyway.

Chairman Tom Davis. That is why I am asking. [Laughter.]

But let me ask you, do we have enough?

Dr. LeDuc. No, we do not have enough. Clearly, we would like to have more. Perhaps Dr. Gellin or Dr. Fauci have better answers, but clearly we do not have enough.

Chairman Tom Davis. Dr. Fauci, do you agree with that?

Dr. Fauci. Yes. We certainly do not have enough right now. We are well aware of that, which is the reason why we are in the process of negotiating to get more. What the right number is, Mr. Chairman, it really is very difficult, if not impossible, to give that. You have heard different groups who have estimated cover 50 percent of the population, cover 25 percent of the population. It is very difficult to determine what the right number is. I think the question you asked and the important point is that 2.3 million treatment doses is not enough and we have to get more, and that is the direction we are heading.

What problem we have is that the actual capacity to make it in a timely manner when you are having demands from other countries and other agencies throughout the world is also something that is problematic.

Chairman Tom Davis. Aren't other countries now trying to get more of this? That is I guess the point that you were trying to make.

Dr. Fauci. Yes. So it makes it important for us to get our bid in now, yes.

Chairman Tom Davis. Dr. Gellin, would you agree with that?

Dr. Gellin. I agree. Let me add to that that as I mentioned, we are in active discussions with all the companies that make all these products, both vaccines and anti-virals, because we are concerned about the capacity to manufacture surge capacity in the available supplies. You will likely hear from the drug company Roche in the second panel that they have recognized this, and after many discussions they have begun to develop a U.S. supply chain. So I think that part of what we are hearing about are many countries order-
ing in this case Tamiflu, but at the same time my understanding is that there is expanding capacity to make that drug.

I also mentioned in my brief remarks that we are also exploring the acquisition of the other neuraminidase inhibitor, zanamivir. It is a similar molecule. It has a slightly different set of clinical indications. It has given as an inhalation rather than oral. We think it is important to diversify that as well. It is more complicated to deliver that drug, but it is also important because of the potential emergence of resistance is that it potentially has a different resistance profile, so it would give us some backup.

Chairman Tom Davis. Dr. Fauci, currently FluMist, which is a nasal flu vaccine, is only approved for healthy children and adults from 5 to 49 years of age. As you know, we have talked about this before. Is there any research underway to consider the broader use of MedImmune’s FluMist beyond the currently approved groups to help alleviate demand for injectable vaccines?

Dr. Fauci. The answer is yes. We are in active discussions with the MedImmune people about trying to get the clinical information available to expand the usages of FluMist because it really is quite a good vaccine. It is a potent vaccine. It induces an even broader range of immunity than the kill dose. So it would behoove us to go in that direction and hopefully we will be able to do the appropriate studies to expand that usage beyond the current approval.

Chairman Tom Davis. Are there other anti-virals besides Tamiflu that might be effective against avian flu? Is NIH researching alternatives to Tamiflu or ways to speed up production of Tamiflu?

Dr. Fauci. Currently, the neuraminidase inhibitors are the only drugs, anti-virals that appear to be effective against the H5N1. I mentioned in my statement just a few minutes ago of the resistance to the amantadine sub-group of M2 inhibitors which is the other class of anti-virals.

What we are doing in research, Mr. Chairman, is we are doing studies to try and determine if combinations of Tamiflu plus the amantadine in a resistant strain to amantadine might actually enhance the anti-viral effect. There is a good history in anti-viral drugs that when you have drugs to which a particular microbe are individually resistant and when you use them in combination, you get a pretty good effect. We see that with HIV and we see that sometimes in tuberculosis.

So we are doing those studies, and we are also doing studies to look at alternative targets. The two categories of drugs that I just mentioned are against two major targets: the M2 protein and the neuraminidase. We are looking at inhibition of entry of the virus, as well as other of the pathways in the replication cycle of the virus.

Chairman Tom Davis. Thank you.

Mr. Waxman.

Mr. Waxman. Thank you, Mr. Chairman.

The three witnesses before us are the good guys. They are trying to figure out what to do for our Nation against the threat of a pandemic flu, but I do not believe they are getting the support they need. Last fall, we had a severe shortage in flu vaccines. Our na-
tional health officials were caught completely unprepared. There were long lines for vaccines and widespread chaos and confusion.

When we examined what went wrong, we learned that the Department of Health and Human Services had ignored warning after warning that we were unprepared to cope with the vaccine shortage. Instead of leadership, our planning was characterized by complacency and false assurances.

So my question today is: Can we prevent the same fiasco from happening again? Dr. Gellin, in your testimony, well, you are the Director of the National Vaccine Program Office and Chair of the Secretary's Influenza Preparedness Task Force. Are we as prepared as we should be to face the threat of a pandemic?

Dr. GELLIN. Preparedness is not an absolute. I think it is clear to say that the efforts that have gone on even on my watch in my brief tenure as the Director of the National Vaccine Program Office have put us in a much better situation of preparedness. Not that I am responsible for those, but I think that it attests to much of what is going on. So there are clearly many more things that we can do and many things that we are doing, specifically around the vaccine piece.

Mr. WAXMAN. Let me ask you some questions about the plan.

Dr. GELLIN. Sure.

Mr. WAXMAN. You stated in your testimony that the department has been actively revising the draft pandemic preparedness and response plan. This is something that has been going on for a long time. As you acknowledge, the 2004 version of the draft contained many holes in key policy areas. Are you actively working to fix these key gaps? Will the new draft contain information on how vaccines will be purchased and distributed? Will the draft address prioritization of scarce supplies of vaccine and anti-viral drugs?

Dr. GELLIN. The clear answer to all those questions is yes. I think that it is important to recognize that the plan is not a skimpy outline. It is a fairly substantial document that we have put on our Web site for public comment last July. The areas you highlighted are specifically areas that we wanted the public to weigh-in on during the public comment period.

As Dr. LeDuc mentioned, we have involvement both from the Advisory Committee on Immunization Practices and the National Vaccine Advisory Committee to provide recommendations so that those critical policy issues can be answered. We cannot have a plan updated without those being addressed.

Mr. WAXMAN. Can you tell us a date by which this report will be released?

Dr. GELLIN. I cannot tell you a date. As mentioned before, it is our expectation that it will be released this summer. There are many moving parts to this and they are converging to the Secretary, who wanted to see it in early August. Subsequent to that, it is our hope to get that out shortly thereafter.

Mr. WAXMAN. Well, the States have been saying they are not getting adequate guidance from the Federal Government. I hope what you finalize will be much more thorough than last year's version.

Dr. GELLIN. As you mentioned in your introductory remarks, what we will have here is the specificity that the States are looking for so they can go on and make their own State-level plans.
Mr. WAXMAN. Dr. LeDuc, I appreciate your observation that the issues of pandemic influenza and annual influenza are linked. You noted that the same laboratories, the same health care providers, the same surveillance system and the same health department plans and personnel will guide both responses.

I would add that these factors link pandemic flu to many other public health issues, not just to annual flu epidemics. That is why I am so concerned the administration is proposing to cut support for local and State health departments by $130 million. The Secretary of the Washington State Health Department will testify in the next panel that these cuts are proposed at exactly the wrong time.

Why are we reducing the ability of State and local health departments to respond to a potential pandemic when health care experts say the risk of a pandemic are increasing? Given the threat of pandemic flu, would it be responsible for Congress to increase support for public health at HHS and in the White House.

In theory, public health is not a partisan issue. In practice, the funding of public health is more contentious, unfortunately, than it should be. What is your response?

Dr. LeDuc. Well, sir, I wholeheartedly support those comments. I could not agree more with your observations. I would just offer a hearty "yes, sir" that these are in fact very serious issues.

I think the threat of pandemic influenza, annual influenza, are just a few examples of the broader issue of emerging infectious diseases, many, many infectious disease threats that are facing the Nation. Clearly, we need a strong capacity at the State and local level to address these issues as a Nation.

Chairman TOM DAVIS. Thank you for your comments.

Mr. GUTKNECHT. Thank you, Mr. Chairman.

Let me just first of all disagree to a certain degree with my distinguished colleague from California, and let me make the point. The last several years, we have heard every year of this impending shortage of vaccine and the potential calamity that would follow thereon. I think in the last several years in every case it has proven not to be quite as serious as we thought.

I think we have to be careful of that. The reason I say that is that more and more the public, if you cry wolf too many times, the public does not take it very seriously. So I think we have to be careful as public policymakers to essentially say that there is a huge public danger. I think there is a serious problem and I think we have to deal with it.

Just for my benefit and I think for the American people, could you just in language that we can all understand explain the difference between an epidemic and a pandemic?

Dr. FauCI. There are technical explanations, but in plain English, an epidemic is when you have a much greater than expected surge of cases within a particular defined geographic location. You could have an epidemic in a particular State or an epidemic in a particular region.
When you are talking pandemic, “pan” being “all,” it is essentially all over the place, in plain English. That is really what a pandemic is.

Mr. GUTKNECHT. Let me come back to some other basics, just again so that I and others understand. What we are really worried about here are viruses that mutate and go from pigs to poultry to people or from poultry to pigs to people. Isn’t that right?

Dr. FAUCI. Yes.

Mr. GUTKNECHT. And I am wondering, and the reason I am going to ask this question, I will tell you a little bit about two laboratories that I have in my district. One is a little medical practice that was started by a fellow by the name of William Worrall Mayo and his two brothers Will and Charlie. They have a pretty sophisticated laboratory there and they are doing some amazing things.

In fact, I was there a couple of months ago and they have a super-computer where they had taken the SARS virus and they showed the three-dimensional representation of the SARS virus, and they have actually tested using the computer the 10 most likely vaccines against the SARS virus, and have determined what they think would be the most viable.

The other is a little laboratory down in Worthington, MN run by some veterinarians. It is called Newport Labs. I will tell you the story, and the reason I tell the story is that what they do is they test animals. People will send cotton swabs in from around the country, and within 24 hours using very sophisticated, I think it is called PCR technology, they will determine what virus it is. More importantly, they will send back to them the right vaccine.

The reason I raise this question, and I think it is important that we continue to develop the vaccines and the other things, but what are we doing to try and, it seems to me if we could vaccinate the pigs and the poultry in Asia, maybe it is just a layman’s view, but if we could keep the disease from ever becoming a pandemic, it would make some sense.

How much are we working with veterinarians and laboratories like that to try and stop the thing before it starts?

Dr. LeDUC. Let me start commenting. Dr. Fauci, I am sure, will have a lot to add.

First with regard to influenza in general, there are many strains and they actually exist in nature in wild birds. So there is basically a silent cycle and a silent reservoir of these strains. That is why Dr. Fauci pointed out that while H5N1 influenza is the current hot topic, we are also concerned about H9N2 and other strains. So there is this silent reservoir of circulating virus that is completely impossible to control.

The decision whether or not to immunize domestic animals as an amplifying host and a link to human transmission is often made on economic basis, in addition to the availability of an intervention of vaccine.

Unfortunately, we do not have the kind of ongoing dialog that we should have between the health sector and the agricultural sector. In an attempt to resolve this problem, we have actually assigned a person to WHO who comes from the agricultural sector. His sole job is to focus on influenza issues and establish a more robust dialog with the FAO and the OIE and WHO to try to approach a co-
ordinated response on how to integrate control both on the agricultural sector as well as the human health sector. So we are trying to work on this.

Dr. Fauci. Just to add to that, to make sure we emphasize that is at the international level. We have good discussion and coordination. In fact, we just had a meeting yesterday at the White House with all of the parties involved, the Department of Agriculture included in that.

But from an international standpoint, I think the critical point that Dr. LeDuc made is it is so tied to the economies of the country that we are going to need a good deal of greater transparency in what is going on in those countries, and a willingness to assume some of the economic burdens and issues that will go along with appropriate culling, appropriate vaccination, getting a good vaccine.

One of the things we are worried about is that if you vaccinate some of the chickens, for example, with a partially effective vaccine, you may mask some smoldering infection. That is superimposed upon with what Dr. LeDuc said about the migratory birds being infected, which is very difficult to get a handle on. It is a very complex issue that at the level of WHO, working very close with the CDC and with the international counterparts, we are trying to address that. But it is a very difficult problem when you have economic considerations very closely tied with that.

Dr. Gellin. If I could add, what you have described and what you have heard from my colleagues is really what is captured in the phrase “emerging infectious diseases,” those that come out of the human-animal interface.

In addition to what Dr. LeDuc mentioned about some of the specific activities, there is also a supplement to the tsunami relief bill that is provided through the Department of State and HHS $25 million to focus on some of the strategic countries in Asia. One of the underlying focal points of that is to do as you described, to bridge the human and animal side so there is a common agenda.

Chairman Tom Davis. Mr. Cummings.

Mr. Cummings. Let me follow up on what Mr. Gutknecht said. I have a question, and something he said was chilling to me. Let me ask you this, gentlemen. In 2001, we had shortages of vaccine for children covering 8 of 11 others; 8 of 11 we did not have. Is that correct? And children died, did they not? Say yes or no, so I can hear you. I mean, it is for the record.

Dr. LeDuc. I believe that is correct, sir.

Mr. Cummings. Children died.

In 2004, we had a shortage of flu vaccine and elderly people waiting in lines. Some of them actually died in line, and 36,000 people die each year from flu. Is that accurate? Come on, gentlemen.

Dr. LeDuc. That is correct, sir.

Mr. Cummings. I am sorry?

Dr. LeDuc. That is correct, sir.

Mr. Cummings. So my question is, do you think that we are crying wolf here? I mean, it is our responsibility as Members of the Congress to protect our citizens. I am just asking you, do you think we are crying wolf here?
Dr. Fauci. No, but let me just add to what I think you are saying. We have discussed and we could reiterate, I certainly have at this committee in the past, and I mentioned it to the chairman as we were giving our statement, there is no doubt that the vaccine enterprise certainly in this country, and you used the word “fragile.” You are absolutely correct. It is not only fragile. It is sort of broke, as it were.

The reason is that there is very little incentive to get vaccine companies involved in vaccine. We discussed this in light of the shortages. We have discussed this in the light of biodefense countermeasures that we need. We have a serious problem. So in that regard, I do not think you are crying “wolf.” We have to fix the vaccine enterprise and make it such that consistently each year we have a predictable and supportable amount of vaccines.

Probably more broke than any of the vaccine sub-groups is the vaccine enterprise associated with influenza because it adds the seasonal uncertainty touch.

Mr. Cummings. Let me ask you this. Dr. LeDuc, the Baltimore Sun recently reported “anti-viral drugs like Tamiflu are essential tool in slowing the spread of disease until a vaccine can be developed to immunize people, a process that can take six to 8 months from the time a killer virus is identified.” Listen to this, “The United States has enough Tamiflu on hand for 2.3 million people,” as you all have testified, “significantly less than some other nations. The United Kingdom, for example, has enough Tamiflu to treat 25 percent of their population, in accordance with the World Health Organization’s recommendation.”

What is the CDC doing to ensure the United States has enough anti-viral drugs to combat a pandemic and identify priority groups who will be most in need of that treatment? And why is it that other countries are able to cover a greater percentage of their people than we are? We have 36,000 people dying a year, and nine times as many people as who died on September 11th.

Dr. Gellin. Let me get back to the heart of your question about the supplies in the stockpile and some of these materials. As I mentioned, and as Dr. Fauci mentioned, we have also been very aggressive about vaccine development. We see the need for both vaccines and anti-virals in the stockpile. You have heard in some detail about where we are going in the clinical trials, the going ahead and manufacturing 2 million doses, the request with manufacturers to make additional vaccine.

At the same time, we have actually bought and secured that amount of anti-viral in the stockpile. There will be subsequent purchases in the near future that are now under discussions with the companies, and additional purchases beyond that.

So it is important to recognize that we are not stopping at 2.3 million. As a point of fact, the other countries have put these other targets out there, not that it is a WHO recommendation per se, but they do not have much of a vaccine strategy right now so they have been putting more of their eggs in that anti-viral basket. We think that we need a balanced strategy as well, but I want to summarize by saying we are not stopping at 2.3 million. You will hear more in the near future about more and subsequently about additional purchases.
Mr. CUMMINGS. Before my time runs out, let me just ask you all this question. The Baltimore Sun recently reported about a pandemic flu simulation that occurred in my district, an affluent county, Howard County. A wide range of participants included representatives from the Governor's office and State and local public health officials.

The Sun reported, "It was not just the deaths in the scenario that disturbed them. Medical supplies were in short supply; absenteeism was soaring; police, firefighters, medical workers and air traffic controllers were among the thousands of sick, dead or terrified; hospitals and mortuaries were overwhelmed; the first small batches of the vaccine were arriving, but they were reserved for health care and public safety workers; crowds gathered demanding vaccination, and small riots were breaking out."

I just want your reaction to that, when we talk about our State and local folks, because they are on the front lines.

Dr. GELLIN. Indeed, they are on the front lines. I read that newspaper when it was on the stand. I think that depicts a number of the concerns about what a pandemic could do, which is why I believe that the plan will provide better guidance for the States as far as how they go about this, and the subsequent purchases of additional materials will help as well.

This all builds on the level of preparedness that has been encouraged by other funding, so I believe that these States are better prepared than they were before all this started.

Mr. CUMMINGS. Thank you, gentlemen.

Mr. SHAYS. Mr. Chairman.

Chairman TOM DAVIS. Yes, Mr. Shays.

Mr. SHAYS. Thank you.

I thank our witnesses again, and I thank you for holding this hearing.

I would like to know when does HHS propose to have a final version of an epidemic preparedness plan? Let me just throw these other questions out. Do you anticipate finalizing the plan before the 2005–2006 annual flu season? Are there practices and guidance in epidemic planning that are relevant should we experience another flu vaccine shortage this year?

Dr. GELLIN. Let me start with that. The plan, and I would be willing to loan you my copy of our draft plan, will be finalized this summer and it will include the specific guidance the States and localities are looking for. It will also include some of the strategic policy issues such as priority-setting when there are short supplies of vaccines and anti-virals. So all those will be done this summer in advance of the flu season.

Dr. LEDUC. If I could just add to that, actually this afternoon the ACIP is going to engage in discussions on the guidance on vaccine and anti-viral drug prioritization and their comments will then roll over to end back later on next month as well. So this really is a very timely discussion and we hope to have the final draft to the Secretary by the first of August. So we are moving along on this.

Mr. SHAYS. OK. Now, the draft plan only addresses HHS's activities. Correct? Yes. Given the broad nature of a pandemic and its impact on commercial agriculture, homeland security, and just society in general, does the administration have plans for government-
wide coordination and has anyone outside HHS been designated as
the lead for orchestrating this coordination?

Dr. GELLIN. As Dr. Fauci mentioned just a few minutes ago, this
coordination has been quite active. Within the Department of
Health and Human Services, Secretary Leavitt sort of influenced
the task force to deal with both pandemic influenza and annual in-
fluenza, given their relationships. There is a process that has really
been coordinated by the White House to assure that there is broad
input by all the departments that have a piece of this. I think in
part it will also follow on to the national response plan for which
there is likely to be a pandemic supplement.

Mr. SHAYS. One of the things that I am struck by is that Dr.
Fauci when you said we just really do not know how many vaccines
are the appropriate number. Is that correct?

Dr. FAUCI. I was referring to drugs, Mr. Shays.

Mr. SHAYS. OK.

Dr. FAUCI. I was asked what the right number of drugs was. We
have 2.3 million treatment doses, and the question was what is the
right number. I said clearly 2.3 million treatment doses is not
enough.

Mr. SHAYS. What I am struck by, it seems to me by now we
would almost have formulas that would come into play. First off,
clearly this is the reason it is a pandemic, in that it is worldwide.
Correct?

Dr. FAUCI. Right.

Mr. SHAYS. And obviously then we have a great deal at stake in
what other countries do. The more vaccines that are out there
worldwide, the less people in the United States will contract it.
Correct?

Dr. FAUCI. Right, yes.

Mr. SHAYS. But isn't there a formula that tells you that?

Dr. FAUCI. The answer, Mr. Shays, is yes there are. There are
mathematical models. The difficulty with the mathematical model
as in all mathematical models, they are totally based on what the
assumptions are that you put into the model. When you get pre-
dictions about how many people will get infected versus who will
get sick, the range is enormous. It goes from 89,000 to several hun-
dreds of thousands of people. If you are going to base who you are
going to treat, treat sick people.

So if you have such a variability, then the number of doses you
will need for sick people is going to be widely variable. Then you
make the decision about is there going to be enough for health
workers, and those formulas are easy because you know how many
health workers you have. Are you going to have treatment avail-
able to incentivize health workers to come to work in the middle
of a pandemic flu? That number is pretty easy to get.

The number that is the big variable is what is going to be the
infection burden among people in this country. We have looked at
those models. Obviously, it is greater than 2.3 million. Some say
it is as high, in our own group, as 20 million treatment doses.

Mr. SHAYS. How long does a vaccine last?

Dr. FAUCI. Vaccine differs from therapy. Therapy shelf-life is
about 5 years for Tamiflu. A vaccine, if you store it well it can last
for a few years. The difficulty with vaccines is that the nature of
flu is that it keeps changing, so it is not a shelf-life issue. It is an effectiveness issue.

Mr. SHAYS. Thank you, Mr. Chairman.

Chairman TOM DAVIS. Mr. Ruppersberger.

Mr. RUPPERSBERGER. Let me have 5 minutes. There are three issues I would like to get into. No. 1 is planning. Congressman Shays got into it. I want to get into a little more specifics, the issue of injection devices, which I think are very relevant because it might be a way for us to use less vaccine and it might even be better. I think we need to look at that.

Also the issue of Tamiflu as it relates to children. Is there clinical testing going on right now? Let me get to that real quick. Where are we with Tamiflu and children?

Dr. FAUCI. Tamiflu is approved for children greater than 1-year-old for treatment and in individuals 13-plus years for prophylaxis. We are in the process of discussions of clinical trials to gather more information, particularly about the safety of Tamiflu in children 2 years of age and younger.

Mr. RUPPERSBERGER. I also understand that you are having problems with the industry as it relates to Tamiflu; that you are not getting the support that you need. Is that still the case?

Dr. FAUCI. I would say more that we are in active discussions trying to get that.

Mr. RUPPERSBERGER. I think that is really something that we need to deal with from an adversary point of view. If you want to lay it out now, I think we should discuss it because if industry is not cooperating, then we are putting everyone at risk, including the children. Where are we with respect to that issue, other than just saying “discussions?”

Dr. FAUCI. We are just in discussions, sir. I am not trying to evade the question. I checked with my staff yesterday and they said we are in active discussions about how we are going to get that information.

Mr. RUPPERSBERGER. It seems to me it should be aggressive discussions.

Dr. FAUCI. We, the NIH, are in an aggressive discussions.

Mr. RUPPERSBERGER. OK. Let me get to planning. In August, the administration released a draft, you probably have it there, you talked about your being before the Commerce Committee or whatever, saying you will have the draft this summer. You just testified to that.

Now, there were key elements in the first draft that were not addressed. I think we can all say that a key element of preparing for a flu pandemic is having a plan. Would you agree with that?

Dr. FAUCI. Absolutely.

Mr. RUPPERSBERGER. OK. Now, if that is the case, the areas that we are missing were undecided questions including how vaccines will be paid for and distributed; second, how scarce supplies of vaccines and drugs will be prioritized; and three, what messages will be communicated to the public in different stages of the pandemic.

Will they be addressed in the plan that you are coming up with this summer, those three elements?

Dr. GELLIN. Yes, to all.
Mr. RUPPERSBERGER. OK. I want to ask this question, too. I do not want to embarrass you because we want to move forward, but it seems to me that why don’t we have a plan now? Canada finalized their plan in 2004. The United Kingdom finalized their plan in March 2005. Why is it taking us so long to get from the draft stage to the final plan?

Dr. GELLIN. We put out a draft last year and we left those areas open honestly to engage public discussion. We are disappointed with the lack of public input. We received few more than 50 comments to the plan that was posted in a 60-day period, because we thought that these areas, particularly the priority groups, were so important because as a pandemic could likely affect everybody in America, let alone everybody around the world, that we wanted to hear what people had to say and what the stakeholders had to say.

When we did not get much from that, we set up a process through the National Vaccine Advisory Committee and the Advisory Committee on Immunization Practices to begin to process that. There is a discussion this afternoon in Atlanta about that, and there is a joint meeting which I believe is the first joint meeting ever of these two Federal advisory committees in mid-July to come up with these recommendations to provide the Secretary.

Mr. RUPPERSBERGER. When you are talking about the health, safety and welfare of people, and then the media picks up on something, a lot of times the issue gets larger than maybe it is. But we cannot take any risks. I mean, we cannot take it for granted that there is not going to be a problem. I really think that it is important for the mindset of the industry, which is part of you all, to really start prioritizing and really do things quickly, and then communicate that to the public.

I can understand your answer about getting people to testify and doing it right, but as it relates to what is happening with flu, and now we hear about the bird issue, and that we really do not know what to do until it happens, are we ready to go, do we have the instrumentalities necessary.

With that, I want to get into injection devices. We talk a lot here about how much inventory we are going to have as far as the vaccine, but where are we with respect to injection devices? First thing, how many injection devices will be necessary to provide for the pandemic flu vaccine for the U.S. population? Can you answer that, anybody?

Dr. GELLIN. If it is the entire population, and we believe that there is going to be a requirement for possibly two doses, that number would be 600 million.

Mr. RUPPERSBERGER. Do you have a plan you can provide this committee on what these devices would be like? Do we have the technology necessary to make sure that they will do the job? Are we ahead of the curve as it relates to the rest of the world, as it relates to injection devices? And finally, do they work? Is it going to make it more efficient and using less of the flu vaccine if we use these devices instead of the needles that we use now?

Mr. SHAYS [presiding]. That will have to be the last question answered.
Dr. GELLIN. OK. There are several questions in there. Let me get to what I believe is the most interesting part of what you ask, and I may ask Dr. Fauci to back me up on that.

There is a global capacity for vaccine production of about 300 million doses of the trivalent vaccine. If you are going to make a single strain vaccine, so instead of three strains, a single strain, that could give you globally in a year maybe 900 million doses. That is the global industrial capacity.

Therefore, some of these devices that I think you are getting to might allow us to actually use less antigen per dose, and effectively stretch that global supply.

Dr. Fauci may want to get into some of this. The conversations they are having with the companies now to do those studies. There was one report in the New England Journal of Medicine last year which are promising, but we need to make sure these things work and provide the immune response that they need to.

Dr. FAUCI. We are actually in discussions about doing trials with different approaches, interdermal versus inter-muscular. Inter-muscular is simple needle-use. Injected interdermal, you can make it much more consistent if you have a needle.

Of course, it is not very difficult, but it requires some training to get the injection into the skin, which is what we called intra-dermal. That requires a different kind of an approach. We are in negotiations about doing a trial comparing one to the other. That does not address directly the question of how many of these devices are going to be available. It is more the proof of concept of whether or not you can use them.

Mr. SHAYS. Thank you.

The gentleman is right. Five minutes is not much time, but he had 7 minutes.

Mr. RUPPERSBERGER. Mr. Chairman, could I just ask for the record, not a question, but put a question for the record?

Mr. SHAYS. Sure.

Mr. RUPPERSBERGER. Do you think that the intra-dermal delivery of influenza vaccine has the potential to improve our preparedness for a flu pandemic?

Mr. SHAYS. And right after we find the answer to that question, we will throw it out, and before you leave we would like you to answer that question.

Mr. DENT.

Mr. DENT. Thank you, Mr. Chairman.

Good morning. I represent an area very close by, the Aventis plant up in Swiftwater, PA, and of course the flu issue is a big deal where I live, as it was in many communities. It caused me to think quite a bit about what lessons have we learned from this past season’s flu vaccine shortage as far as distribution, prioritization and communication between State and local health officials, and what can we do to be better prepared for when an actual pandemic occurs, not just one that is naturally occurring, whether it be a flu, but perhaps some genetically engineered pathogen that could be injected by some non-state actor, from a homeland security standpoint. Can you just tell us the lessons that you have learned?

Dr. LEDUC. Thank you very much for that question, sir. Clearly, the challenges that we faced with the influenza vaccine availability
last year brought home several lessons, one of which is the critical importance of communication and active partnership with State and local health departments and partners as the situation evolves.

Another lesson is the real need for real-time communications on what is going on. Concurrently with that, a need for real flexibility because these issues we really do not have control over a lot of the situations that we are faced with. In that regard, we also learned that it is important to have plans in place up front that look at a variety of potential outcomes, especially with regard to delivery of flu vaccine in this particular case.

The other issue that we learned was that if we try to use a non-licensed product under an investigation of new drug application, that becomes very problematic. It is difficult to implement those.

Finally, I think the other lesson we learned is that it is very, very difficult to get the public to accept influenza vaccine beyond December of the calendar year.

Dr. Fauci. There is another issue also, I just might add to that. It has to do with a question that I answered in response to Mr. Cummings’ question. That is the vaccine enterprise and how fragile it is. What we do need is American companies making vaccine on American soil. We have foreign countries making it in Swiftwater. We have American companies making it in Liverpool. What we need is to have a greater commitment on the part of our own industrial partners here in the United States so that we can have a steady flow, and understanding of that each year.

Mr. Dent. What was your understanding as to why the vaccine flu was not being produced up in Swiftwater where they have the capacity to do so?

Dr. Fauci. No, no, Swiftwater is doing a terrific job. They were our sole source this past year.

Mr. Dent. Correct.

Dr. Fauci. No, the point I’m making is that we need to incentivize more companies to get involved in influenza vaccine manufacturing and production. That is what we really need.

Mr. Dent. How would you incentivize those companies?

Dr. Fauci. Well, we have discussed again before this committee and other committees a number of things. There are several issues that have to do with financial incentives, and even stabilizing the influenza market, as it were. The CDC and the department has been trying over the past couple of years to get a greater number of people each year to routinely get vaccinated. We used to do 50 million or 60 million. We got it up to 80 million. We tried to get it to 100 million last year. We in fact probably need to go up to 150 million to 180 million.

Once we do that, then you have a stable pool of people who will be getting vaccinated, which makes it much more attractive to industry to get involved in a stable market, as opposed to a market where they do not know from 1 year to another whether they are going to have to throw away 10 million doses.

There are other incentives regarding liabilities and things like that we have spoken about in the past.

Mr. Dent. Thank you. No further questions.

Mr. Shays. Thank you.

Mrs. Maloney.
Mrs. Maloney. You are the guys trying to help us solve this problem. I represented a city that really was in crisis when we did not have the vaccines. It was really terrible. We want to prevent that.

I think, Dr. Fauci, you hit it on the head when you said we have to produce it right here in the United States. One of the problems is we had to fly over to England. Then there were these questions about their standards, are they the same as ours, and all other kinds of things.

I guess we need to figure out how to handle this better. I guess I just want to hear any other ideas about how we can stockpile it here in the United States, it you cannot manufacture it, and then at least have the stockpile here. And do we have the budget in place to make these purchases?

One of the problems we had in the last crisis is that we could not buy it or we did not have the money to buy it, and there were all kinds of problems about making sure that when we were buying it overseas, it did meet the health standards of the United States, and how can we plan that better? Obviously, it would be better to manufacture it in the United States, but if we are not manufacturing it in the United States, how can we guarantee that we are going to have several people manufacturing it so that if one person has a problem in maintaining certain standards, there is another place we can go to.

I guess an important question is the budgeting. Do we have the budget to buy a stockpile and to put in place the planning for it.

I would like to start with Dr. Fauci and anyone else who would like to answer.

Dr. Fauci. Thank you, Mrs. Maloney. That is a lot of questions there. Let me just take one of them to answer because it relates to what I just mentioned a moment ago, is how are we going to get these companies involved. That relates to the incentives that we need. We need a stable pool of people. We need protections against the liabilities that they face. We may even need things like tax incentives to build plants in the United States.

The issue of stockpiling, I will make a quick comment then I am sure that Dr. LeDuc can comment on that since the CDC is involved in small stockpiling issue each year.

Unlike other pharmaceuticals, it is very difficult to long-term stockpile influenza vaccine because even in a non-pandemic situation, it changes a bit from year to year, so almost invariably we have to deal with a small, sometimes moderate modification of the vaccine from year to year. So stockpiling for influenza just does not work in the big picture. You need a little stockpile the way the CDC has for the emergency situations, but a broader stockpile is just not tenable when you are dealing with a changing virus from year to year.

Dr. LeDuc. I would just agree with those comments. Stockpiling is not the solution to this particular problem for influenza. I think, as Dr. Fauci and Dr. Gellin have both said, the real issue is the fragility of our vaccine enterprise, and we really need to address that.

Dr. Gellin. If I could comment, I think it is important to look at some of the changes in the marketplace. In 1990, as a Nation,
we used less than 30 million doses of influenza vaccine. That has been ratcheted up over time and there are a variety of reasons why that has been the case, but as a Nation, we have never used more than 83 million doses, while the CDC recommends that more than twice that many people receive an annual flu shot for their own personal health benefits.

Nevertheless, those numbers have increased dramatically. At the same time, I do not have the pricing information, the price has gone up; the reimbursement rates by CMS have gone up. It has become a more interesting marketplace for many manufacturers. We have seen this, and I think maybe it was last year that provided an opportunity for many more manufacturers to come and discuss with us. Dr. Fauci mentioned NIH working with GSK to produce some of the data, so they have brought their license application.

So I am hopeful that we will have more manufacturers to the marketplace in the near future.

Mrs. MALONEY. My time is almost up. I just would like to throw out, obviously we do not have time to get manufacturing going in our own country, so what are we going to do for next year? Last time, we only had one manufacturer, as I recall, that we were working with in England, and they were not up to our standards.

Are we contracting now with certain manufacturers in other countries for just this coming year? This is a long-term problem. We hear you and we are going to try to do something about it, but this flu season will be coming quickly and we do not have time to adjust in the United States. We are going to be dependent on foreign importation again, and how are we planning on that?

Dr. FAUCI. We have Sanofi-Pasteur standard, which was successful interaction with the last year. Chiron is getting back. It is a bit unclear exactly how many doses they are going to be able to give us, but there is a range of doses. We have been working with GlaxoSmithKline from the previous year about trying to get them in the market for X amount of doses, not exactly certain. So we now have at least three companies, in addition to MedImmune with their FluMist. So it is not just the single company for this coming year.

Mrs. MALONEY. Thank you. My time is up.

Mr. SHAYS. I thank the gentlelady.

We will turn now to the former chairman of this committee, Dan Burton.

Mr. BURTON. It is nice seeing you gentlemen again.

First of all, I want to congratulate you on addressing this issue. I think it is very important. I think we are all concerned about a major flu epidemic that might be started by radicals to try to destroy this country, or at least a part of it.

The question I would like to ask you deals with another subject. I know that you are aware that for about 4 or 5 years we held hearings when I was chairman of this committee on the mercury in the vaccines. I am very much in favor of the vaccine programs. I think they have given us the highest quality of life in the history of mankind. But we have gone from 1 in 10,000 children who are autistic, and I know there are questions about how you define somebody that is autistic and they split hairs on this, but we are now, according to CDC, at 1 out of 166 children that are autistic.
We had scientists and doctors before the committee when I was Chair that told us that there was no doubt in their minds, and these are not just fly-by-night doctors and scientists, these are people from all over the world that believe that one of the major contributing factors of the autism and the epidemic of autism was the mercury in the vaccines.

Recently, Robert F. Kennedy, Jr., wrote an article which talks about meetings that took place in secret with our health agencies and some of the pharmaceutical companies. I will be happy to get you a copy of that. Have you seen that article? Do you know what I am talking about?

So there is a great deal of concern among people in this country about the mercury in the vaccines and the effect of that and what it is going to do to people long term, especially the kids who are going to live a long life and many of whom will be disabled because of the autism or neurological disorders.

But we are here today to talk about the flu vaccine. Every Member of Congress that I know of that is concerned about flu. At my age, we get a flu vaccine shot. I have gotten mine this year, even though I knew there was mercury in it. We still have thimerosal in most of the adult vaccines. Many of the scientists that came before this committee told us that not only did the mercury in the vaccines contribute to neurological disorders in children, but they believed it also had an adverse impact on older folks and could be a contributing factor in neurological problems such as Alzheimer's disease.

So I would just like to ask you, why don't we get the mercury out of all vaccines? It is not necessary. I know that they use because they use it in 10- or 20-shot vials for production purposes, but we could go to single-shot vials and eliminate that. I would like to know what our health agencies are doing about getting mercury, which is a very toxic substance, out of all vaccines.

In my district, we had a small breakage of a container that contained mercury. It was not much more than what would fill this cup. They evacuated two square blocks of people and brought in the fire department people to clean it up in uniforms that looked like they were from outer space. It was because mercury is so toxic.

Here in Washington, DC, they spilled some mercury in a high school laboratory and they burned all the children's shoes and clothes and everything else and got everybody out of the school while they cleaned up the mercury in that room.

So we know mercury is one of the most toxic substances in the world. It makes no sense to me to continue to have it in our vaccines. There is a growing body of evidence and scientists that believe that the mercury in the vaccines contributes to these neurological disorders in children and adults, and I would like for you to tell me today you are going to get it out of all vaccines. So, can you give me an answer, gentlemen?

Dr. LeDUC. Bruce might have more information, but you are right, sir. The single-dose vaccines for pediatrics, for I think all childhood vaccines, are free of mercury.

Mr. BURTON. There are three that still have mercury in them, three children's vaccines still have mercury.
Dr. LeDUC. I stand corrected then. I know at least the material that we have purchased for the stockpile for influenza is free of thimerasol.

The multi-dose vials, you are correct, continue to have a trace amount of thimerasol as a preservative in it. I do not have an answer as to how industry is going to work through that. Perhaps my colleagues do.

Dr. FAUCI. Certainly the ultimate goal is just what you are saying, Mr. Burton, is to get it out of all of the vaccines. The difficulty we are facing with influenza is the double problematic issue of trying to rev up and make it in as efficient a manner as possible, which really requires multi-dose right now. If to get it in a single dose, it would really be very difficult to meet the goal. That is not an excuse for forgetting about the issue of trying to get a thimerasol-free vaccine ultimately, which is what we are ultimately trying to do. But, unfortunately, it is not going to be for this year's cycle.

Mr. BURTON. If the Chair would bear with me for one more real brief comment. Dr. Fauci, I have high regard for all of you. I know that may seem insincere after all the hearings we have had, but I really do have high regard for all of you and our health agencies. I think you are doing the Lord's work by trying to protect this country. But we have been talking about getting mercury out of vaccines for at least 10 years, and it seems to me that the health agencies could put pressure on the producers to come up with an alternative to what we are using to make sure these vaccines are safe in multi-shot vials. Either that, or going to a production system that will create single-shot vials. And if we did that 5 years ago, 4 years ago, we wouldn't be talking about, oh, we can't do it right now on the flu vaccine.

So I really hope and I pray for the health of these people that are having these neurological problems—and the ones who will have them in the future—that we get on with the program and get mercury out of all vaccines as quickly as possible.

Thank you, Mr. Chairman.

Mr. SHAYS. I thank the gentleman.

Ambassador Watson.

Ms. WATSON. I want to thank the Chair and also the panelists for coming here, talking about influenza and our preparation. What I noticed last year is that we were scrambling around, and since Chiron admitted that its supply was contaminated, that put us in a very bad position and we saw people who really needed to get their shots, not being able to access the shots, and had to wait in long lines for hours, particularly our seniors.

So my question for Dr. Bruce Gellin is how are we planning if we run into this situation again—and I have been listening very intently. It seems like the supply is limited and we can't keep a supply over a period of time, and we seem not to have been able to buildup the capability to produce the solutions here for the shots. So what are we doing? How are we planning to take care of those in need? Who goes to the top of the list; where do they go; and what are our plans if this occurs again? That is question No. 1.

Dr. GELLIN. You ask all the relevant questions, the same questions my mother asked me when she called me from a grocery store
in Central Connecticut, asking how long the line was going to be. As we have highlighted, this is clearly a fragile business, and the disappointment we had last year when we lost half of our supply forced us to redistribute it.

I think the good news in that story was when we look back over the past year, we found that we actually did a pretty good job of getting it to high-risk people, and the messages of if you are at lower risk, step aside. I think there were some adjustments made to allow that to happen. Clearly, a large part of this, as you mention, is about communication, so should there be such an issue, it is very clear who is prioritized and the need to better communicate with both the health care community and the public health community about the distribution.

So I think that the lesson last year has put that part of the operation—which is largely the CDC—in place. At the same time, we have regular discussions with the manufacturers along the line so we can keep track of where they are in their anticipated supply over the year, and have mapped out just a few scenarios about how we would adjust things and how priority groups might be determined based on those supply situations.

Ms. Watson. I was quite amazed last year that we didn’t have a plan in place. What is further amazing me is the reasons why—and I think you were addressing those when I walked into the hearing—we have not developed the capability in this country, why we have not, decades ago, done the research to test the flu vaccines, and why we cannot manufacture. I understand that it is Canada and Great Britain that do the majority. Correct me if I am wrong. But we certainly have the ability to do that.

Is it a misplaced priority? Are we looking at other issues, rather than the protection of our people? Flu can kill, and it kills tens of thousand annually. And I don’t know why we are not on top of it. Can someone enlighten me? What did I miss?

Dr. Gellin. I can’t speak to the history, but I can speak to the present. I believe that, in point of fact, the largest single manufacturer of influenza vaccine in the world is in Pennsylvania. There are maybe a dozen or so companies. We have one, Sanofi Pasteur, which is based in Pennsylvania, that I believe produces the single most influenza vaccine in one facility.

Ms. Watson. For our country or others?

Dr. Gellin. For our country.

Ms. Watson. Well, what is the problem, why do we run short?

Dr. Gellin. Well, we have more needs than that one manufacturer can make, which gets me to where we are now and what we are doing ahead. And I think it was the attention being paid to pandemic influenza, or some strategic investments, and Dr. LeDuc was mentioning about surge capacity. We have done a few things to shore up our supply, particularly with pandemic in mind. We have made sure that, in this case, Sanofi, has all the eggs that they need 24 hours a day to make as much vaccine as they can in a year. That was not a system they had in place beforehand. It is a seasonal disease and it is a seasonal vaccine, and we filled in that. So should they need, on any day of the year, to make vaccine at full capacity, they now have the eggs in place to do that.
But, more importantly, the next step is trying to think about the kinds of capacity and the kinds of production technologies that may improve where we are. Eggs have served us well, but they have some limitations, and we have put significant funds to try to accelerate the development of new technologies that can allow what we described as surge capacity and more vaccine to be produced.

And, finally, to that point, in addition to developing these vaccines, accelerating the development, getting them licensed, part of the criteria to this funding stream is to develop facilities so that ultimately these new vaccines will be produced in the United States.

Ms. Watson. OK, I am sorry, I am out of time. I was just going to join with my friend, Congressman Dan Burton, on the mercury issue and the slow movement that has taken place slowly in trying to improve.

So there are other questions, too, but I know I am out of time, Mr. Chairman.

Mr. Shays. Thank you.

Ms. Watson. Thank you for the time.

Mr. Shays. We have another that is a rather large panel, so we will get to that and just thank all of our witnesses. We will be following up with some questions. Mr. Burton may have some; I know the committee does. Ambassador Watson may as well, and the ranking member and others may. So thank you all very much.

We will announce our second panel. It is Dr. Crosse, Director of Health Care Issues, U.S. Government Accountability Office; Ms. Selecky, Washington State Secretary of Health, testifying on behalf of the Association of State and Territorial Health Officials; Dr. Hearne, executive director, Trust for America’s Health; Dr. John Milligan, executive vice president and chief financial officer, Gilead Sciences, Inc.; and Mr. Abercrombie, president and chief executive officer, Hoffman-La Roche, Inc., accompanied by Dr. Dominick Iacuzio, medical director, Roche Laboratories.

We have enough seats for everyone there? Stay standing, if you would, because we are going to swear you in.

[Witnesses sworn.]

Mr. Shays. Note for the record our witnesses have responded in the affirmative.

And we will start with you, Dr. Crosse, and we will just go right up.

Dr. Crosse. Thank you.

Mr. Shays. Five minutes is the time allotted. Obviously, if you go over a minute or two, we can live with that. But we have a large panel and a busy schedule today. Thank you.

Dr. Crosse.